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REACTION BETWEEN UNSATURATED COMPOUNDS AND ORGANIC MAGNESIUM COMPOUNDS.

XII.—ALDEHYDES AND KETONES.

BY E. P. KOHLER.

In the first paper[1] of this series I described the results obtained by allowing excess of various organic magnesium compounds to react with α,β-unsaturated ketones that have phenyl in combination with the carbonyl group. A comparison of these results with those obtained by Grignard[2] and by Klages[3] led to the inference that the behavior of phenyl ketones is different from that of methyl ketones. This conclusion was supported by an experiment in which benzalacetone was treated with phenylmagnesium bromide, and by some observations made while studying the behavior of unsaturated esters.[4] The difference in the behavior of the two classes of ketones was represented by the equations:

[1] THIS JOURNAL, **31**, 642.
[2] Ann. Chim. Phys. [7], **35**, 477.
[3] Ber. d. chem. Ges., **35**, 2651.
[4] THIS JOURNAL, **33**, 21.

I. $C_6H_5CH:CHCOCH_3 + RMgX =$
$C_6H_5CH:CHC(R)(CH_3)OMgX \rightarrow$
$C_6H_5CH:CHC(R)(CH_3)OH;$

II. $C_6H_5CH:CHCOC_6H_5 + RMgX =$
$C_6H_5(R)CHCH:C(C_6H_5)OMgX \rightarrow$
$C_6H_5(R)CHCH_2COC_6H_5.$

The importance of these results was evident, but before they could be used for testing the various theories relating to unsaturated compounds it was necessary to determine whether all unsaturated ketones behave either like methyl or like phenyl ketones, or whether, by systematically changing the hydrocarbon residues, it would be possible to get substances that would give both of these typical reactions. Ketones reacting in both ways were soon found. Experiments with these showed that the amounts of 1,2- and 1,4-addition with Grignard's reagent depend upon a number of things—the nature of the unsaturated compound, the number and arrangement of the hydrocarbon residues, the character of the magnesium derivative, and, possibly, temperature, concentration, and solvent. In order to determine the relative importance of these factors it has been necessary to make and compare a great variety of unsaturated compounds and to repeat some of the experiments with Grignard's reagent previously made, both by myself and by others. The results of this work are described in this paper.

Special attention was paid, in all experiments, to the amounts of the various products, but even so, no very great accuracy can be claimed except in those cases in which only one substance is formed. The two products most commonly formed—unsaturated alcohol and saturated ketone—cannot be determined directly. The alcohol almost invariably loses water when distilled under diminished pressure and the resulting hydrocarbon generally boils so nearly at the same temperature as the ketone that it is not possible to separate the two without so much loss of material that the results are valueless.

In the preliminary experiments I tried transforming the ketone into oxime and then separating oxime and hydrocar-

bon by vacuum distillation, but found that at some stage in this process either the unsaturated alcohol or the hydrocarbon undergoes polymerization, forming high-boiling products that cannot be separated from the oximes. I decided, therefore, to destroy the unsaturated products by oxidation with permanganate and weigh only the ketone. Unless otherwise specified in the experimental part, the procedure was as follows:

A suitable quantity of the unsaturated compound was added, slowly and with constant shaking, to a large excess of the reagent which was cooled in a freezing mixture. The resulting magnesium derivatives were poured on ice as soon as the colored intermediate compounds had completely disappeared. After dissolving basic salts with iced hydrochloric acid, the ethereal layer was removed, the aqueous layer extracted with ether, and the combined ethereal solutions dried over calcium chloride. The ether was then distilled and the residue dissolved in acetone, to be treated with potassium permanganate. In order to avoid the necessity of using large quantities of solvent, the permanganate was added in the form of a very fine powder. By using glass beads and shaking vigorously, just as reliable results are obtained with the powder as with a solution. During the oxidation the temperature was kept below 20° with running water. Excess of permanganate was removed with sulphur dioxide dissolved in acetone. In the trial experiments the oxides of manganese were dissolved with aqueous sulphur dioxide but it was found that the ketones are easily and completely removed by washing the precipitated oxides with hot acetone.

The following experiments were made to test the constancy of the results:

I. Thirty grams of benzalethylmethyl ketone were added to a solution obtained by dissolving 11 grams of magnesium in ethyl bromide and ether. The product decolorized 33 grams of permanganate and yielded 24.2 grams of ketone.

II. Thirty grams of the same ketone were added to a solution obtained by dissolving 11 grams of magnesium in ethyl iodide and ether. The product decolorized 34.5 grams of permanganate and yielded 23.9 grams of ketone.

III. Sixty grams of the ketone were added to a solution of 18 grams of magnesium in ethyl bromide and ether. The product decolorized 65 grams of permanganate and gave 49.1 grams of ketone.

As most ketones present no greater difficulties than the one used, it is clear that the method is sufficiently accurate for the purpose of comparison.

The quantitative results obtained with two magnesium compounds are summarized in the following table, which begins with acrolein, the simplest substance that contains the chain C:C.C:O, and ends with tetraphenylpropenone, in which all the hydrogen atoms of acrolein have been replaced by phenyl. The numbers in columns I. and II. express the percentage of the unsaturated compound represented by the amount of 1,4-addition product that was obtained. For the sake of comparison I have added two substances that contain triple linkages:

	With C_6H_5MgBr.	With C_6H_5MgBr.
$CH_2:CHCHO$	0	0
$CH_3CH:CHCOCH_3$	75	40
$\begin{matrix}CH_3\\ \quad\diagdown\\ \quad\ C:CHCOCH_3\\ \quad\diagup\\ CH_3\end{matrix}$	0	0
$C_6H_5CH:CHCOCH_3$	60	12
$C_6H_5CH:CHCOCH_2CH_3$	71	40
$C_6H_5CH:CHCOCH\begin{matrix}\diagup CH_3\\ \diagdown CH_3\end{matrix}$	100	88
$C_6H_5CH:CHCOC\begin{matrix}\diagup CH_3\\ -CH_3\\ \diagdown CH_3\end{matrix}$	100	100
$CH_3OC_6H_4CH:CHCOCH_3$	63	13
$C_6H_5CH:CHCOCH:CHC_6H_5$	91	73
$C_6H_5CH:CHCOCH_2CH\begin{matrix}\diagup C_2H_5\\ \diagdown C_6H_5\end{matrix}$	100	93
$C_6H_5CH:CHCOCH_2CH\begin{matrix}\diagup C_6H_5\\ \diagdown C_6H_5\end{matrix}$	100	99
$CCl_3CH:CHCOC_6H_5$	—	95
$C_6H_5CH:CHCOC_6H_5$	99	94

	With C_2H_5MgBr.	With C_6H_5MgBr.
$CH_3OC_6H_4CH:CHCOC_6H_5$	98	96
$C_6H_5CH:CHCOC_6H_4OCH_3$	100	99
$C_6H_5CH:CHCOC_6H_2(CH_3)_3$	—	100
$C_6H_5CH:CBrCOC_6H_5$	100	100
$C_6H_5CH:C(CH_3)COC_6H_5$	100	100
$C_6H_5CH:C(C_6H_5)COC_6H_5$	100	100
$(C_6H_5)(CH_3)C:CHCOC_6H_5$	44	41
$(C_6H_5)_2C:CHCOC_6H_5$	18	0
$(C_6H_5)_2C:CHCOC_6H_2(CH_3)_3$	?	0
$C_6H_5CH:C(C_6H_5)COC_6H_5$	?	0
$C_6H_5CH:C(C_6H_5)C\equiv N$	100[1]	58
$C_6H_5C\equiv C(C_6H_5)COC_6H_5$	—	0

The table shows that while aldehydes form only unsaturated alcohols most ketones form both unsaturated alcohols and saturated ketones. Results somewhat similar to these were obtained by Posner,[2] who studied the behavior of unsaturated ketones towards mercaptans. He found that two reactions are possible—saturation of the ketone and condensation with the carbonyl group. The former, as suggested by Posner, is probably due to 1,4-addition:

I. $C_6H_5CH:CHCOCH_3 + C_2H_5SH =$
$C_6H_5CH(SC_2H_5)CH:C(CH_3)OH \rightarrow$
$C_6H_5CH(SC_2H_5)CH_2COCH_3$.

The latter may be represented as follows:

II. $C_6H_5CH:CHCOCH_3 + 2C_2H_5SH =$
$H_2O + C_6H_5CH:CHC(SC_2H_5)_2CH_3$.

[1] Nitrile formed by 1,4-addition.
[2] Ber. d. chem. Ges., **34**, 1395.

The only significant difference between these reactions and those with Grignard's reagent is that in the case of mercaptans the second reaction may take place with the product of the first. After a careful study of a considerable number of unsaturated ketones, Posner concluded that all the facts can be explained by the variable activity of the carbonyl group. The factors that, in his belief, diminish the activity of this group are the double linkage in the α,β-position and hydrocarbon residues. Of the latter he writes:[1] "The more completely the hydrogen atoms in combination with the carbon atoms that participate in the double linkage or that adjoin the carbonyl group are replaced by hydrocarbon residues, the less the tendency of carbonyl to condense with mercaptans and the more favorable the conditions for the formation of monosulphones."

Posner's explanation seems inadequate. That the double linkage in the α,β-position has no peculiar influence in diminishing the activity of carbonyl is shown by the behavior of dibenzalacetone and benzaldiphenylbutanone towards phenylmagnesium bromides. The former gives about 27 per cent of tertiary alcohol, the latter 1. The saturated residue, therefore, diminishes the activity of the carbonyl group more than the unsaturated, and the difference is such as would be expected between a straight and a branched chain of this character. The statement with reference to the effect of hydrocarbon residues is too general because it includes both of the unsaturated carbon atoms. Hydrocarbon residues in the β-position, doubtless, slightly diminish the activity of the carbonyl group, but they do not favor 1,4-addition. This seems clear after comparing the results obtained from ethylideneacetone with those obtained from mesityl oxide, or those from benzalacetophenone with those obtained from triphenylpropenone.

In my opinion, the products obtained are the result of two independent reactions that proceed at relatively different rates in different ketones because they are not determined by the same factors. Only one of the rates depends directly

[1] Ber. d. chem. Ges., 35, 801.

upon the reactivity of the carbonyl group. The influences that affect this can be estimated from measurements that have been made with saturated ketones. Stewart[1] and Petrenko-Kritschenko[2] measured the rate of addition of acid sulphites to aldehydes and ketones, and discovered an interesting relation between the rate of addition and the complexity of the compounds. The rates of oxime-[3] and hydrazone-formation[4] have also been measured. The results show that the relative rates at which different ketones form oximes and hydrazones are approximately the same as those at which the same ketones combine with acid sulphites. It is probable, therefore, that oximes and hydrazones are formed in steps, only one of which—the addition-reaction—is measurable:

$$R_2CO + NH_2OH = R_2C(OH)NHOH \rightarrow R_2C{:}NOH + H_2O.^5$$

By combining the results obtained with bisulphites, hydroxylamine, and phenylhydrazine, it is possible to arrange acetaldehyde and a number of methyl ketones in the order of their activity in addition reactions. If the assumptions made above are permissible, this order would not be changed by the introduction of an unsaturated residue into the methyl group, provided that the same residue is introduced into all of the ketones. In the following table the first column of numbers gives the percentage of sodium bisulphite addition-product formed in the first forty minutes, the second the percentage of oxime formed in ten minutes, the third that of phenylhydrazone formed in one hour, and the last the percentage of tertiary alcohol obtained by treating the benzylidene derivatives of the same substances with phenylmagnesium bromide:

	1.	2.	3.	4.
CH_3CHO	88.7	....	....	100
CH_3COCH_3	53.6	45.1	66	88
$CH_3COC_2H_5$	29.1	36.6	52	60
$CH_3COC_3H_7$	....	34.7	38	42

[1] J. Chem. Soc., **87**, 185.
[2] Ann. Chem. (Liebig), **343**, 163.
[3] Ber. d. chem. Ges., **34**, 1702. J. Chem. Soc., **87**, 410.
[4] Ann. Chem. (Liebig), **343**, 154.
[5] Stewart: *Loc. cit.*

	1.	2.	3.	4.
$CH_3COCH(CH_3)_2$	9.4	31.4	15	12
$CH_3COC(CH_3)_3$	5.6	12.9	3.6	0
$CH_3COC_6H_5$	0	8	3.7	0
$CH_3COC_6H_3(CH_3)_2$	0	0	0	0

It is evident that the activity of the carbonyl group of unsaturated ketones varies in the same way as that of the corresponding saturated compounds and that this is an important factor in determining the mode of addition of Grignard's reagent. Variations in the activity of this group do not, however, have the same consequences in the different reactions under comparison. The addition of bisulphite to aldehydes and ketones is a reversible process. The activity of the carbonyl group, therefore, determines the composition of the equilibrium and, in practice, the reaction can be completed by using excess of reagent or by removing the product. Oxime and phenylhydrazone formation are in most cases not measurably reversible; hence, the activity of the carbonyl group merely determines the rate.

The reaction between unsaturated compounds is likewise not reversible, but there are two possibilities. The final result, therefore, depends quite as much upon the rate of 1,4-addition as upon the activity of the carbonyl group, and substances in which this activity is approximately the same may give almost totally different products with the same reagent. This is illustrated by the following series, where the reagent was phenylmagnesium bromide:

I. $CH_3CH:CHCOCH_3$ gave 40 per cent $CH_3CH:CHC\begin{cases}CH_3\\OH\\C_6H_5\end{cases}$

60 per cent $CH_3CH(C_6H_5)CH_2COCH_3$.

II. $(CH_3)_2C:CHCOCH_3$ gave 100 per cent $(CH_3)_2C:CHC\begin{cases}CH_3\\OH\\C_6H_5\end{cases}$

0 per cent $(CH_3)_2C(C_6H_5)CH_2COCH_3$.

III. $C_6H_5CH:CHCOC_6H_5$ gave 4 per cent $C_6H_5CH:CHC\begin{cases}C_6H_5\\OH\\C_6H_5\end{cases}$

96 per cent $(C_6H_5)_2CHCH_2COC_6H_5$.

IV. $C_6H_5C(CH_3):CHCOC_6H_5$ gave 41 per cent $C_6H_5C(CH_3):CHC\begin{cases}C_6H_5\\OH\\C_6H_5\end{cases}$

59 per cent $(C_6H_5)_2C(CH_3)CH_2COC_6H_5$.

V. $(C_6H_5)_2C:CHCOC_6H_5$ gave 100 per cent $(C_6H_5)_2C:CH_2C\begin{cases}C_6H_5\\OH\\C_6H_5\end{cases}$

As the activity of the carbonyl in V. is certainly not greater, and probably somewhat less, than in III., the surprising difference in the results can only be due to a diminution in the rate of 1,4-addition, owing to the presence of the second phenyl in the β-position. The interference of the two phenyl groups in this position is so great that when the carbonyl is rendered inactive by the introduction of a hydrocarbon residue in the α-position the result is complete inertness towards phenylmagnesium bromide. This was observed in tetraphenylpropenone, which has phenyl in the α-position, and in diphenylpropionylmesitylene, in which the inactivity of the carbonyl group is due to diorthosubstitution.

The progressive retardation of the two rates of reaction as the hydrogen atoms are replaced, step by step, with hydrocarbon residues is quite noticeable in the performance of the experiments. Aldehydes react energetically at —37°, and the colored intermediate products disappear at once. The replacement of the hydrogen in the aldehyde group with methyl already causes a perceptible loss in activity; the intermediate compounds no longer disappear immediately at —37°, but the reaction still proceeds freely at 0°. When isopropyl or phenyl is introduced in place of methyl, the colored products accumulate at zero, but disappear at the ordinary temperature. When, finally, hydrocarbon residues are also introduced in the β-position the reaction must be completed by boiling.

The diminution in reactivity that is brought about by substitution is generally attributed to steric hindrance, and this is a satisfactory explanation of the facts described in this paper. Stewart and Baly[1] recently discovered an interesting relation between the rate of addition to aldehydes and

[1] J. Chem. Soc., **89**, 618.

ketones and the absorption spectra of these substances in the ultra-violet. They draw attention to what they regard as the shortcomings of the theory of steric hindrance and propose "isorropesis"—a conception based on the relation they discovered—as an explanation for chemical activity. This explanation is also applicable to the facts under consideration, but as an investigation of the absorption spectra of unsaturated aldehydes and ketones is now in progress, I shall defer the application until the results of this investigation are available.

In order to show as clearly as possible how the nature of the unsaturated compound affects the course of the reaction, I have considered, hitherto, only the results obtained with a single reagent. The table near the beginning of the paper shows a considerable difference in the relative amounts of 1,2- and 1,4-addition obtained with ethyl- and phenylmagnesium bromides. Similar results had previously been observed in the case of unsaturated nitriles.[1] The following series, which gives the percentage of ketone obtained by treating benzalethylmethyl ketone with various reagents, indicates that the difference is due to the chemical character of aliphatic and aromatic magnesium compouuds.

CH_3MgBr	70
C_2H_5MgBr	71
$C_2H_5C(CH_3)MgBr$	69
$C_6H_5CH_2MgBr$	68
C_6H_5MgBr	40

The only other factors to be considered are temperature and solvent. For the purpose of detecting any effect due to differences in temperature, equal quantities of benzalethylmethyl ketone were added slowly to corresponding solutions of ethylmagnesium bromide, one of which was kept at —37°, the other at the boiling point. The two solutions gave almost the same amounts of ketone, and a similar result was obtained when the experiment was repeated with phenylmagnesium bromide as the reagent.

It is exceedingly difficult to get trustworthy results in

[1] This Journal, **35**, 386.

solvents other than ether. By Tschelinjeff's[1] method it is easy to prepare organic magnesium derivatives in indifferent solvents, but their insolubility in these solvents interferes with the reaction. It was pointed out in earlier papers that in order to avoid complex products it is generally necessary to use considerable excess of reagent. The concentration of the reagent in most indifferent solvents is so small that it is usually impossible to prevent local excess of unsaturated compound. For this reason the only successful experiments were those carried out in very dilute solutions of benzene and ethyl bromide. In these solvents benzalacetone and ethylmagnesium bromide gave the same results as in ether.

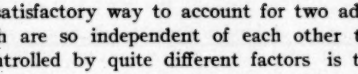
The facts discussed above do not support the current conceptions relating to unsaturated compounds. The simplest and, in many ways, the most satisfactory explanation of the addition reactions of unsaturated substances is that proposed by Thiele.[2] Thiele was the first to recognize the importance of 1,4-addition to compounds that have two double linkages in combination with two adjoining carbon atoms, and he developed his theory of "partial valences and conjugated double linkages" to account for this mode of addition and for the apparent inactivity of two of the unsaturated carbon atoms. At the time only one case was known where a substance containing such a system of double linkages formed more than one addition product with the same reagent. This was cinnamic aldehyde, which gives two products with acid sulphites.

Thiele evidently regarded cinnamic aldehyde as an exception. He concluded that "in some addition reactions the result is affected by influences that at present are indefinable." My results show, however, that the behavior of cinnamic aldehyde is not exceptional, because most ketones give two products with the same organic magnesium compound. This behavior of unsaturated compounds resembles that of tautomeric substances, but in the case of unsaturated ketones it is not possible to explain the results by intermediate compounds, or by assuming that only one of the products is formed directly.

[1] Ber. d. chem. Ges., **37**, 2081.
[2] Ann. Chem. (Liebig), **306**, 87; **311**, 241.

The only satisfactory way to account for two addition reactions which are so independent of each other that their rates are controlled by quite different factors is to assume that these unsaturated compounds are capable of reacting in two modifications. These may be represented by

or without using partial valences by



These formulas are among those used by Knoevenagel[1] to represent his explanation of 1,4–addition on the basis of stereochemistry; but I propose to use them simply as the best means of representing a number of experimental facts, without any reference to space relations. If, as is probable, the change from one modification to the other takes place more rapidly than any addition reactions, then the relative amounts of 1,2- and 1,4-addition products will depend solely upon the rates of addition to the systems I. and II. The relative amounts of these products ought to be independent of the nature of the solvent, because this would affect both rates in the same way. They might vary with the temperature because even for closely related reactions the temperature coefficient is not necessarily the same. The relation between the two rates would, however, depend mainly upon the atoms or groups located at different parts of the chain and upon the character of the addenda. This follows from the behavior of saturated carbonyl compounds and that of ethylene derivatives which have only one double linkage.

By adopting formulas like those proposed or, better perhaps, by recognizing that in the addition reactions of substances containing the conjugated system, C:C.C:O, the outcome is the resultant of two simultaneous reactions that proceed independently, a much more satisfactory explanation for the behavior of these substances can be given than has hitherto been possible. An examination of the literature

[1] Ann. Chem. (Liebig), **311**, 215.

bearing on the subject discloses many results that appear to be contradictory. These are due to secondary reactions that mask the additive processes. Nearly all reactions involving 1,2-addition to carbonyl are reversible, and all products formed by 1,4-addition, except those obtained with Grignard reagents, immediately undergo rearrangement into saturated compounds that are still capable of 1,2-addition to carbonyl. As a result, the products ultimately obtained do not represent the relative rates of addition but the relative stability of the substances under the conditions of the experiment.

The reaction between cinnamic aldehyde and acid sodium sulphite, for example, takes place, mainly, as represented by the equation

I. $C_6H_5CH:CHO + HNaSO_3 \rightleftharpoons C_6H_5CH:CH(OH)SO_3Na.$

A small quantity may react according to the equation

II. $C_6H_5CH:CHCHO + HNaSO_3 = C_6H_5CH(SO_3Na)CH:CHOH \rightarrow C_6H_5CH(SO_3Na)CH_2CHO.$

In the absence of secondary reactions the product would be composed of oxysulphonate mixed with a small quantity of saturated aldehyde, but as the first reaction is reversible under the conditions of the experiment while the second is not the product of the first reaction slowly but completely passes into that of the second. For this reason the latter is the only substance obtained when equimolecular quantities of the reagents are allowed to remain in contact until the change is complete. In the meanwhile, however, a third reaction takes place, owing to the rearrangement of the 1,4-addition product:

III. $C_6H_5CH(SO_3Na)CH_2CHO + HNaSO_3 \rightleftharpoons C_6H_5CH(SO_3Na)CH_2CH(OH)SO_3Na.$

As this reaction is reversible, like the first, the product ultimately disappears, but by interrupting the reaction before it is complete it is easy to get all three products, and the relative amounts obtained in this way do not repre-

sent the relative ease with which 1,2- and 1,4-addition is accomplished; they depend entirely upon the time of interruption.

The reaction between unsaturated ketones and hydroxylamine represents a still more complicated case in point. The two primary processes are represented by the equations

$$\text{I. } RCH{:}CHCOR + NH_2OH \rightleftharpoons RCH{:}CHC(R)(OH)NH_2OH \rightleftharpoons H_2O + RCH{:}CHC(R){:}NOH.$$

$$\text{II. } RCH{:}CHCOR + NH_2OH = RCH(NHOH)CH{:}C(R)OH \rightarrow RCH(NHOH)CH_2COR.$$

The first reaction is reversible at every step, hence under favorable conditions the product of this reaction may pass completely into that of the second reaction, but under other conditions as, for example, when it is fixed in the form of hydrochloride, it may remain unchanged. The result, therefore, depends upon whether the reaction takes place in neutral or acid solution. The product of the first reaction, moreover, contains a new conjugated system that may react with a second molecule of hydroxylamine and form an oxaminooxime according to the equation

$$\text{III. } RCH{:}CHCR{:}NOH + NH_2OH = RCH(NHOH)CH{:}C(R)NHOH \rightarrow RCH(NHOH)CH_2C(R){:}NOH.$$

The primary product of the second reaction immediately undergoes rearrangement into an oxamino ketone that may also react with a second molecule of hydroxylamine. When results depend so largely upon experimental conditions as these do, it is, of course, impossible to draw trustworthy conclusions either as to the course of the reaction or as to the nature of unsaturated compounds.

The reaction between unsaturated compounds and organic magnesium compounds is not reversible and both of the addition products are stable. For this reason it has been possible not only to prove conclusively that one of the products is formed by 1,4-addition but also to get a definite conception

of the factors that determine the mode of addition to conjugated systems.

EXPERIMENTAL PART.

Acrolein.

The acrolein used in the following experiments was made by heating glycerin with boric acid, as directed by Wohl and Neuberg.[1] This method gives an excellent yield, but to get a perfectly pure aldehyde is much more difficult than is indicated by the statements of the authors. My product, after purification in accordance with their directions, boiled at 48°–56° and repeated fractional distillations with an efficient still-head were necessary to get a constant boiling point of 52°–53°.

Reaction with Ethylmagnesium Bromide.—An ethereal solution of 100 grams of acrolein was added very slowly to a similar solution of the reagent made from 80 grams of magnesium and cooled in a freezing mixture. The resulting magnesium derivative was immediately decomposed with iced acid and the ethereal layer separated and shaken, mechanically, for ten hours with a freshly prepared, saturated solution of potassium bisulphite. As no solid separated, the bisulphite solution was drawn off, the ether pumped out of it, and the residue distilled after addition of excess of sodium carbonate. No organic substance passed into the distillate, thus proving the complete absence of aldehydes in the product. The ethereal layer was dried, the ether removed, and the residue distilled under diminished pressure. The result was 122 grams of ethylvinylcarbinol, boiling at 114°–116°, and about 20 grams of a colored residue that was probably a polymerization product of the alcohol, because it lost water on distillation.

Reaction with Phenylmagnesium Bromide.—This reaction was recently described by Klages.[2] My experiment was carried out exactly like that with ethylmagnesium bromide. The bisulphite test showed that the product was entirely free from aldehyde. The only substance obtained was phenyl-

[1] Ber. d. chem. Ges., **35**, 3166.
[2] *Ibid.*, **39**, 2552.

allyl alcohol, boiling at 124°–125° (30 mm.), and under ordinary pressures at 215°–216°. The same substance was obtained by Klages.

Ethylidenacetone.

Ethlylidenacetone was made by condensing acetaldehyde with acetone and eliminating water from the product. The condensation was carried out as directed by Claissen,[1] but instead of purifying the intermediate product, the entire fraction distilling at 70°–90° (20 mm.) was boiled with an equal weight of acetic anhydride. This procedure saves both time and material because it is easier to purify the unsaturated ketone than the aldol condensation product. The yield was 113 grams from 1 kilogram of aldehyde and 2 kilograms of acetone.

Reaction with Methylmagnesium Bromide.—An ethereal solution of 35 grams of the ketone was added to a cooled solution of the reagent containing 20 grams of magnesium. After decomposing the product with ice and removing the magnesium salts and ether there remained 42 grams of a colorless liquid that boiled at 108°–114°. Half of this liquid was dissolved in ether and shaken for five hours with excess of a saturated solution of sodium bisulphite. The ethereal layer, after washing and drying, gave 4.2 grams of liquid that boiled, constantly, at 112°, readily decolorized a solution of bromine in chloroform and reduced potassium permanganate at the ordinary temperature. This product was evidently dimethylisoallylcarbinol, formed by addition of the reagent to carbonyl. The bisulphite layer was treated with excess of sodium carbonate and distilled until the residue was odorless. The distillate was saturated with potassium carbonate and extracted with ether. It yielded 14.2 grams of a colorless liquid that boiled at 115° and was indifferent to permanganate. This was methylisobutyl ketone, formed by 1,4-addition.

The other half of the product was dissolved in acetone, cooled with ice-water and treated with permanganate. The salts and oxides of manganese were removed by filtration and the solution in acetone fractioned. It yielded 16 grams

[1] Ber. d. chem. Ges., **32**, 1352.

of methylisobutyl ketone. Both methods of separation show that about 75 per cent of the product is a ketone formed by 1,4-addition.

Reaction with Ethylmagnesium Bromide: *ε-Keto-γ-methylhexanone*, $C_2H_5CH(CH_3)CH_2COCH_3$.—The procedure was the same as with methylmagnesium iodide, but as the tertiary alcohol lost water below 100° the entire product was treated with potassium permanganate. The result was 19.5 grams of saturated ketone from 20 grams of ethylidenacetone.

Analysis:

0.1420 gram substance gave 0.3817 gram CO_2 and 0.1504 gram H_2O.

	Calculated for $C_7H_{14}O$.	Found.
C	73.68	73.31
H	12.28	12.40

The ketone is a mobile liquid boiling at 146°–147°. It readily combines with sodium bisulphite, forming a product that is oily at the ordinary temperature but solidifies in a freezing mixture.

Reaction with Phenylmagnesium Bromide: *β-Phenylmethylpropyl Ketone*, $CH_3CH(C_6H_5)CH_2COCH_3$.—The entire product of the reaction from 40 grams of unsaturated compound was treated with potassium permanganate dissolved in acetone. The residue left after removing oxides of manganese and acetone was fractioned under diminished pressure. It gave 30 grams of ketone, boiling at 132° (22 mm.).

Analysis:

0.1368 gram substance gave 0.4068 gram CO_2 and 0.1083 gram H_2O.

	Calculated for $C_{11}H_{14}O$.	Found.
C	81.48	81.10
H	8.64	8.79

The ketone forms a very unstable crystalline addition product with sodium bisulphite.

Phenylpentanonoxime, $CH_3CH(C_6H_5)CH_2C(CH_3) : NOH$.—The oxime was obtained by boiling an alcoholic solution of the ketone with hydroxylamine hydrochloride and potassium

hydroxide and distilling the product under diminished pressure. It is a viscous liquid boiling at 160° (20 mm.).

Analysis:

0.1601 gram substance gave 0.4367 gram CO_2 and 0.1253 gram H_2O.

	Calculated for $C_{11}H_{18}ON$.	Found.
C	74.57	74.39
H	8.53	8.69

Mesityl Oxide.

The reaction between mesityl oxide and Grignard's reagent has been studied by Grignard[1] and by v. Fellenberg.[2] Grignard, using methylmagnesium iodide, obtained 70 per cent of the calculated yield of dimethylpentadiene, formed by loss of water from an intermediate tertiary alcohol. v. Fellenberg, by distilling under very low pressures, obtained the alcohol itself. As these investigators had no reason to suspect the possibility of 1,4-addition, I repeated the experiment but used a large excess of reagent in order to prevent the formation of complex products.

Ethereal solutions containing 200 grams of ketone and the ethylmagnesium bromide obtained from 70 grams of magnesium were brought together very slowly in a freezing mixture. The product, separated in the usual way, was divided into two portions, one of which was boiled with alkaline solution of hydroxylamine while the other was treated with permanganate dissolved in acetone. Two grams of the portion that had been boiled with hydroxylamine and subsequently washed and dried were tested for nitrogen in the usual way. No nitrogen was found. The remainder was distilled under diminished pressure and the residue left after removing the hydrocarbon again tested for nitrogen, but with the same result as before.

The treatment with permanganate also showed that the product contained no ketone. The acetone left after salts and oxides of manganese had been removed was distilled with an efficient still-head. It boiled at 56°–57°, leaving only a small

[1] Compt. rend., **130**, 1324.
[2] Ber. d. chem. Ges., **37**, 3578.

quantity of residue. When this was digested with semicarbazide it gave 0.3 gram of a crystalline semicarbazone, but the analyses showed that this was derived from some very complex product. It seems certain, therefore, that no 1,4-addition takes place in the case of mesityl oxide.

Benzalacetone.

Grignard[1] added benzalacetone to methylmagnesium iodide and obtained phenylmethylbutadiene—a solid melting at 27°. Later, Klages[2] added the same ketone to methylmagnesium iodide and ethylmagnesium bromide and obtained "a good yield" of unsaturated hydrocarbons. It is probable that his products were impure, because he describes phenylmethylbutadiene as a liquid, and his analytical results for the corresponding ethyl derivative are too low. In the first paper[3] of this series I described an experiment which showed that the principal product with phenylmagnesium bromide is methyldiphenylpropenol. A repetition of all these experiments on a larger scale has shown that some ketone, due to 1,4-addition, is formed in each case and that with aliphatic magnesium compounds this is the principal product.

Reaction with Ethylmagnesium Bromide.—An ethereal solution of 60 grams of benzalacetone that had been carefully purified by recrystallization from ether was added to ethylmagnesium bromide made from 18 grams of magnesium and kept cool in a freezing mixture. The resulting liquid was immediately poured on cracked ice and treated with iced hydrochloric acid. The ethereal layer was dried, the ether removed, and the residue distilled under diminished pressure. The result was 68 grams of a liquid boiling at 126°–130° (18 mm.) and 2 grams of a thick paste boiling above 180°, evidently a complex product.

Analyses showed that the liquid boiling at 126°–130° was a mixture, but it was not possible to separate it completely by distillation. The entire product was therefore dissolved in acetone and treated with potassium permanganate as

[1] Ann. Chim. Phys. [7], **24**, 486.
[2] Ber. d. chem. Ges., **35**, 2651.
[3] This Journal, **31**, 642.

long as this was reduced below 15°. The residue left after removal of the oxides of manganese and of acetone boiled at 130° (18 mm.) was indifferent to permanganate and did not decolorize a solution of bromine in chloroform. The yield of ketone was 41 grams.

Analysis:

0.1202 gram substance gave 0.3605 gram CO_2 and 0.0995 gram H_2O.

	Calculated for $C_{12}H_{16}O$.	Found.
C	81.85	81.78
H	9.09	9.19

Phenylhexanonoxime, $C_2H_5CH(C_6H_5)CH_2C(CH_3):NOH$.—To prove that the substance is a ketone it was dissolved in alcohol and boiled with excess of hydroxylamine hydrochloride and potassium hydroxide. The product, purified by vacuum distillation, was a colorless liquid boiling at 170° (20 mm.), mobile when hot, but very viscous at the ordinary temperature.

Analysis:

0.1606 gram substance gave 0.4169 gram CO_2 and 0.1233 gram H_2O.

	Calculated for $C_{12}H_{17}ON$.	Found.
C	75.38	75.49
H	8.90	9.09

These results show that about 60 per cent of the product obtained by treating benzalacetone with ethylmagnesium bromide is a saturated ketone formed by 1,4-addition. Two additional experiments were made for the purpose of testing the constancy of the ratio between ketone and hydrocarbon. In one 30 grams of unsaturated ketone were added to excess of ethylmagnesium bromide, in the other the same amount of ketone was added to ethylmagnesium iodide. In each case the entire product was treated with permanganate without previous distillation. The first experiment gave 22.2 grams, the second 21.6 grams, of phenylhexanone. The ratio is, therefore, constant and it is not influenced by the nature of the halogen.

Reaction with Phenylmagnesium Bromide: β,β-Diphenylethylmethyl Ketone, $(C_6H_5)_2CHCH_2COCH_3$.—The experiment

was made with 240 grams of ketone and 72 grams of magnesium dissolved in brombenzene. Half of the product was distilled under diminished pressure, but this method of separation proved unsatisfactory. The liquid began to distil at 170° (20 mm.) and the temperature rose steadily to 280° (20 mm.) when the distillation was interrupted.

The remainder of the product was dissolved in acetone and treated with potassium permanganate. The acetone solution, freed from oxides of manganese, was distilled with steam. The distillate contained benzene, formed by the action of water on excess of reagent, a small quantity of brombenzene and 11 grams of diphenyl. The residue left in the distilling flask was dissolved in ether and the solution dried with sodium sulphate and fractioned under diminished pressure. It gave 18 grams of ketone boiling at 194° (20 mm.). This represents about 12 per cent of the original ketone.

Analysis:

0.1414 gram substance gave 0.4480 gram CO_2 and 0.0916 gram H_2O.

	Calculated for $C_{18}H_{18}O$.	Found.
C	85.71	85.44
H	7.14	7.19

Diphenylethylmethyl Ketoxime, $(C_6H_5)_2CHCH_2C(CH_3):NOH$. —The oxime was made by boiling an alcoholic solution of the ketone with hydroxylamine hydrochloride and potassium hydroxide and distilling the product under diminished pressure. The distillate, collected from 220°–222°, solidified on standing. The solid was powdered and boiled with ligroin (30°–50°). This extracted a product that, after several recrystallizations from ligroin containing a small quantity of ether, separated in plates melting at 91°. The residue left after extraction was crystallized from ether, from which it separated in lustrous needles melting at 128°. It is readily soluble in all common organic solvents except low-boiling ligroin. The following analyses show that these two products are isomeric oximes.

I. 0.1521 gram substance (91°) gave 0.4467 gram CO_2 and 0.0999 gram H_2O.

II. 0.1690 gram substance (128°) gave 0.4970 gram CO_2 and 0.1119 gram H_2O.

	Calculated for $C_{18}H_{17}ON$.	Found. I.	II.
C	80.33	80.09	80.11
H	7.11	7.29	7.35

Benzalethylmethyl Ketone.

Reaction with Ethylmagnesium Bromide: *Phenylheptanone*, $C_2H_5CH(C_6H_5)CH_2COC_2H_5$.—The procedure was the same as with benzalacetone. The product was distilled, first under diminished pressure, when it boiled at 135°–140° (20 mm.), then under ordinary pressure, boiling point 250°–255°. It was plainly a mixture, but separation by distillation was impracticable with the quantity of material available. The experiment was therefore repeated and the product at once treated with potassium permanganate dissolved in acetone. The unoxidized compound boiled at 142° (17 mm.).

Analysis:

0.1511 gram substance gave 0.4537 gram CO_2 and 0.1312 gram H_2O.

	Calculated for $C_{13}H_{18}O$.	Found.
C	82.10	81.88
H	9.49	9.64

β-Phenylheptanone is a mobile liquid that boils without decomposition at 255°. The yield—24 grams from 30 grams of unsaturated ketone—represents approximately 70 per cent of the possible amount. The oxime, made like those described previously, is a very viscous liquid boiling at 172° (18 mm.).

Analysis:

0.1417 gram substance gave 0.3955 gram CO_2 and 0.1211 gram H_2O.

	Calculated for $C_{13}H_{19}ON$.	Found.
C	76.05	76.12
H	9.27	9.49

Reaction with Isobutylmagnesium Bromide: *Methylphenyloctanone*, $C_2H_5CH(CH_3)CH(C_6H_5)CH_2COC_2H_5$.—The experiment was made with 30 grams of unsaturated ketone and the

entire product dissolved in acetone and treated with permanganate. The residue left after removing oxides of manganese and acetone was distilled under diminished pressure. It yielded 23.5 grams of ketone boiling at 152° (17 mm.). This amount is very little less than that obtained with ethylmagnesium bromide.

Analysis:

0.1402 gram substance gave 0.4231 gram CO_2 and 0.1300 gram H_2O.

	Calculated for $C_{15}H_{22}O$.	Found.
C	82.57	82.30
H	10.10	10.31

The oxime is a viscous liquid boiling at 185°.

Analysis:

0.1420 gram substance gave 0.4011 gram CO_2 and 0.1280 gram H_2O.

	Calculated for $C_{15}H_{23}ON$.	Found
C	77.25	76.89
H	9.87	10.00

Reaction with Phenylmagnesium Bromide: *Diphenylpentanone*, $(C_6H_5)_2CHCH_2CO_2C_2H_5$.—The experiment was performed with 100 grams of unsaturated ketone. Half of the product was fractioned under diminished pressure. After losing water freely at about 180° it began to distil at 203° (20 mm.), but the temperature rose to 285°, where the distillation was interrupted. There was a large quantity of highly colored residue, indicating extensive polymerization of the unsaturated hydrocarbon.

The remainder of the product was dissolved in acetone and oxidized with excess of permanganate. The oxides of manganese were filtered off and extracted with boiling water. From the aqueous solution hydrochloric acid precipitated a mixture of solid acids. These were dried and extracted with ligroin (30°–50°). The ligroin, on evaporation, left almost pure benzoic acid. The residue, after recrystallization from water, melted at 132°. This was α,α-phenyloxypropionic acid, because it gave propiophenone when warmed with sulphuric acid. The product of the reaction therefore contained

some diphenylpentenol, which was oxidized as represented by the equation:

$$C_6H_5CH:CHC(C_2H_5)(C_6H_5)OH + 4O = C_6H_5COOH + C_6H_5(C_2H_5)COHCOOH$$

The filtrate from the oxides was freed from acetone and distilled under diminished pressure. It was thus separated into two substances boiling at 120°–123° (35 mm.) and 225° (35 mm.). The first of these was propiophenone. It boiled at 214°–216°, solidified on cooling, melted at 20°–21°, and gave an oxime melting at 53°. As α,α-phenyloxypropionic acid is not readily oxidized by permanganate dissolved in acetone, this seems to indicate the presence of an allene hydrocarbon.

$$C_6H_5CH:C:C(C_2H_5)C_6H_5 + 5O = C_6H_5COOH + CO_2 + C_6H_5COC_2H_5.$$

An analysis of the high-boiling distillate showed that this was diphenylpentanone, formed by 1,4-addition. The yield of ketone was 60 grams, representing 40 per cent of the unsaturated ketone.

Analysis:

0.1552 gram substance gave 0.4884 gram CO_2 and 0.1076 gram H_2O.

	Calculated for $C_{17}H_{18}O$.	Found.
C	85.71	85.82
H	7.56	7.69

Diphenylpentanone is a colorless liquid boiling without decomposition at 334°–335°. When digested with an alkaline solution of hydroxylamine it gave a mixture of stereoisomeric oximes. These were separated from each other by crystallization from aqueous alcohol, in which the high-melting oxime is sparingly soluble. One is deposited in needles melting at 146°, while the other separates slowly in large, lustrous plates melting at 117°.

Analysis:

I. 0.1214 gram substance (146°) gave 0.3590 gram CO_2 and 0.0850 gram H_2O.

II. 0.1112 gram substance (117°) gave 0.3290 gram CO_2 and 0.0752 gram H_2O.

	Calculated for $C_{17}H_{19}ON$.	Found. I.	II.
C	80.63	80.64	80.68
H	7.50	7.77	7.56

Benzalmethylisopropyl Ketone.

Reaction with Ethylmagnesium Bromide: *Phenylmethylheptanone*, $C_2H_5CH(C_6H_5)CH_2COCH(CH_3)_2$.—The reaction was carried out with 30 grams of unsaturated ketone and the whole product treated with potassium permanganate dissolved in acetone. It reduced less than 1.5 grams of the permanganate. The oxides of permanganate were extracted with boiling water, the filtrate evaporated to small volume and acidified. From the solution, ether extracted only a small quantity of benzoic acid.

The acetone solution was rectified under diminished pressure. It gave 32 grams of ketone, a mobile liquid boiling at 138° (15 mm.).

Analysis:

0.1268 gram substance gave 0.3829 gram CO_2 and 0.1144 gram H_2O.

	Calculated for $C_{14}H_{20}O$.	Found.
C	82.35	82.15
H	9.80	10.01

The oxime was made in the usual way and purified by distillation under diminished pressure. It was obtained as a very gummy liquid boiling at 175° (18 mm.).

Analysis:

0.1331 gram substance gave 0.3753 gram CO_2 and 0.1174 gram H_2O.

	Calculated for $C_{14}H_{21}ON$.	Found.
C	76.71	76.89
H	9.59	9.80

Reaction with Phenylmagnesium Bromide: *Diphenylmethylpentanone*, $(C_6H_5)_2CHCH_2COCH(CH_3)_2$.—Thirty grams of ketone were used in the experiment. The product was distilled with

steam until free from brombenzene and diphenyl, then dissolved in acetone and treated with permanganate. It reduced 12 grams of permanganate and the aqueous extract of the oxides of manganese yielded 6.5 grams of benzoic acid, showing that about 10 per cent of the product was tertiary alcohol. The filtrate from the oxides of manganese, when distilled under diminished pressure, gave 37.5 grams of ketone boiling at 210° (18 mm.). The distillate solidified on standing.

Analysis:

0.1228 gram substance gave 0.3855 gram CO_2 and 0.0835 gram H_2O.

	Calculated for $C_{18}H_{20}O$.	Found.
C	85.71	85.70
H	7.94	7.77

Diphenylmethylpentanone is readily soluble in organic solvents. It separates from ether and from ligroin in large, colorless prisms, melting at 66°. When boiled with an alkaline solution of hydroxylamine it gives a mixture of two isomeric oximes. These were separated by fractional crystallization from aqueous alcohol. One separated in needles melting at 151°, the other in large plates melting at 99°.

Analysis:

I. 0.1225 gram substance (151°) gave 0.3614 gram CO_2 and 0.0854 gram H_2O.

II. 0.1410 gram substance (99°) gave 0.4178 gram CO_2 and 0.0985 gram H_2O.

	Calculated for $C_{18}H_{21}ON$.	Found. I.	Found. II.
C	80.90	80.48	80.81
H	7.86	7.74	7.76

α-Brom-β,β-diphenylmethylpentanone, $(C_6H_5)_2CHCHBrCOCH(CH_3)_2$.—Bromine reacts slowly with a boiling solution of diphenylmethylpentanone in chloroform, but the result is an oily mixture that is separated with difficulty. An excellent yield of the bromine substitution product was obtained by treating the magnesium derivative with bromine. Fifty grams of benzalmethylisopropyl ketone were added to a solution of phenylmagnesium bromide that was

made from 15 grams of magnesium. The mixture was boiled for 10 minutes, then cooled in a freezing mixture. Bromine that had been dried over phosphorus pentoxide was added to this until the color of the liquid showed excess. Most of the product separated in crystalline form when the mixture was poured into iced acid. The solid was removed and the filtrate distilled with steam. The residue was added to the solid previously obtained and the whole purified from absolute alcohol. The yield was 80 grams of pure product.

Analysis:

0.2256 gram substance gave 0.5387 gram CO_2 and 0.1210 gram H_2O.

	Calculated for $C_{18}H_{19}OBr$.	Found.
C	65.25	65.16
H	5.74	5.51

The substance crystallizes in needles melting at 108°. It is readily soluble in chloroform, moderately in ether and boiling absolute alcohol, sparingly in cold alcohol and ligroin. Like other α-brom ketones that have two phenyl groups in the β-position, it is easily converted into an unsaturated ketone.

Diphenylmethylpentenone, $(C_6H_5)_2C : CHCOCH(CH_3)_2$.—A solution of 16 grams of potassium hydroxide in 8 grams of boiling water was added to 80 grams of bromdiphenylmethylpentanone, dissolved in boiling absolute alcohol and the mixture boiled for two hours. The alcohol was then removed and the residue poured into water. The product separated as an oil. A preliminary experiment showed that this contained a substance that decomposed when distilled under diminished pressure—probably an α-oxyketone formed by replacement of bromine with hydroxyl. Variable quantities of such oxyketones are usually formed when α-bromketones are treated with potassium hydroxides, but as they are readily oxidized by permanganate, while unsaturated ketones that have two phenyl groups in combination with one of the ethylene carbon atoms are oxidized with difficulty, it is easy to remove them. The oil was, therefore, dissolved in acetone and treated with permanganate until reduction no longer took

place rapidly at the ordinary temperature. The residue left after removing oxides of manganese and acetone boiled without decomposition at 210°–211° (15 mm.). The yield was 48 grams.

Analysis:

0.1468 gram substance gave 0.4640 gram CO_2 and 0.0990 gram H_2O.

	Calculated for $C_{18}H_{18}O$.	Found.
C	86.40	86.20
H	7.20	7.42

Diphenylmethylpentenone is a pale-yellow, viscous liquid that does not solidify at —20°. It does not decolorize a solution of bromine in chloroform and it does not reduce permanganate more rapidly than does acetone.

Benzalpinacoline.

Reaction with Ethylmagnesium Bromide: *Phenyldimethylheptanone*, $C_2H_5CH(C_6H_5)CH_2COC(CH_3)_3$.—The product obtained from 30 grams of unsaturated ketone reduced less than half a gram of permanganate. The oxides of manganese were extracted with boiling water, the solution evaporated to small volume and acidified. Carbon dioxide was given off, but no precipitate formed and no benzoic acid or other organic compound was obtained by extracting the acid liquid with ether. It seems clear, therefore, that the reduction was not due to any product formed from the unsaturated ketone but to some impurity introduced either with the ether or with the magnesium derivative.

The solution in acetone, when distilled under diminished pressure, gave 34 grams of ketone boiling at 145° (15 mm.).

Analysis:

0.1460 gram substance gave 0.4411 gram CO_2 and 0.1341 gram H_2O.

	Calculated for $C_{15}H_{22}O$.	Found.
C	82.56	82.41
H	10.09	10.21

The ketone solidified after some time and could be recrystallized by cooling in a freezing mixture a solution in ligroin

(30°–40°) that was saturated at the ordinary temperature. It separated in needles melting at 34°.

With an alkaline solution of hydroxylamine, phenyldimethylheptanone gives a mixture of oximes that is separated with difficulty. The most satisfactory results were obtained by fractional crystallization from ligroin. The higher melting oxime separates in needles melting at 83°, the other in prisms melting at 36°.

Analysis:

I. 0.1671 gram substance (83°) gave 0.4736 gram CO_2 and 0.1504 gram H_2O.

II. 0.1504 gram substance (36°) gave 0.4246 gram CO_2 and 0.1364 gram H_2O.

	Calculated for $C_{15}H_{23}ON$.	I.	Found. II.
C	77.25	77.28	76.98
H	9.87	10.01	10.08

Reaction with Phenylmagnesium Bromide: *Diphenyldimethylpentanone*, $(C_6H_5)_2CHCH_2COC(CH_3)_3$.—The product obtained from 30 grams of unsaturated ketone reduced less than a gram of permanganate and it was found, by the method described under the reaction with ethylmagnesium bromide, that even this small amount of reduction was not due to any product formed from the unsaturated ketone. The solution in acetone deposited 41 grams of solid. After crystallization from aqueous alcohol this melted at 85°.

Analysis:

0.1378 gram substance gave 0.4342 gram CO_2 and 0.1015 gram H_2O.

	Calculated for $C_{19}H_{22}O$.	Found.
C	85.72	85.91
H	8.27	8.20

The ketone crystallizes in aggregates of fine needles. It is readily soluble in alcohol and ether, sparingly in ligroin.

Diphenyldimethylpentenol Acetate, $(C_6H_5)_2CHCH:C(C(CH_3)_3)OCOCH_3$.—Ten grams of acetyl chloride were added very slowly to the magnesium derivative obtained by dropping 10 grams of benzalpinacoline into excess

of phenylmagnesium bromide. The liquid was boiled for an hour, then poured into ice-water and treated in the usual way. The product was purified by crystallization from a mixture of chloroform and alcohol. It separated in brilliant plates melting at 165°.

Analysis:

0.1302 gram substance gave 0.3910 gram CO_2 and 0.0935 gram H_2O.

	Calculated for $C_{29}H_{34}O_2$.	Found.
C	81.81	81.89
H	7.80	7.99

The acetate is readily soluble in chloroform, moderately in acetone, sparingly in alcohol and ether. Alcoholic potassium hydroxide rapidly hydrolyzes it to potassium acetate and diphenyldimethylpentanone.

Diphenylmethyl Ether of Diphenyldimethylpentenol, $(C_6H_5)_2CHCH:C(C(CH_3)_3)OCH(C_6H_5)_2$.—In order to test the reactivity of magnesium derivatives obtained by adding Grignard's reagent to unsaturated ketones having aliphatic groups in combination with carbonyl, benzalpinacoline was allowed to react with phenylmagnesium bromide in the usual way, and the resulting magnesium derivative boiled with various alkyl halides. It was found that the behavior of this magnesium derivative is exactly like that previously observed with phenyl ketones; it does not react with simple halides but reacts very smoothly with diphenylbrommethane. The product was purified by crystallization from chloroform, which deposits it in plates melting at 224°. It is moderately soluble in benzene and chloroform, sparingly in other solvents.

Analysis:

0.1925 gram substance gave 0.6310 gram CO_2 and 0.1280 gram H_2O.

	Calculated for $C_{39}H_{38}O$.	Found.
C	89.09	88.90
H	7.41	7.42

Bromdiphenyldimethylpentanone, $(C_6H_5)_2CHCHBrCOC(CH_3)_3$.—This substance was made by treating the ketone, dissolved in chloroform, with bromine and also by adding bromine to

the magnesium derivative of diphenyldimethylpentenol. The yield is equally good in both cases. The product was purified by adding hot alcohol to its solution in chloroform. It is readily soluble in ethyl acetate and chloroform, moderately in acetone, ether and boiling absolute alcohol. It crystallizes in plates melting at 145°.

Analysis:

0.2011 gram substance gave 0.4881 gram CO_2 and 0.1140 gram H_2O.

	Calculated for $C_{19}H_{21}OBr$.	Found.
C	66.09	66.19
H	6.08	6.29

Diphenyldimethylpentenone, $(C_6H_5)_2C:CHCOC(CH_3)_3$.—It is easy to eliminate hydrobromic acid from the bromine substitution product just described. A strong aqueous solution of potassium hydroxide was added, in small portions, to 175 grams of the substance, suspended in boiling absolute alcohol, until the liquid remained alkaline after boiling for half an hour. The alcohol was then distilled and the residue poured into water. The product was precipitated as an oil, but this solidified completely in the course of a day. The solid was recrystallized from ligroin until it melted sharply at 66°. The yield was 130 grams—almost the calculated quantity.

Analysis:

0.1414 gram substance gave 0.4470 gram CO_2 and 0.0950 gram H_2O.

	Calculated for $C_{19}H_{20}O$.	Found.
C	86.36	86.21
H	7.60	7.46

Diphenyldimethylpentenone crystallizes from ligroin in large, pale-yellow plates. It is readily soluble in all organic solvents, except ligroin. It does not combine with bromine at the ordinary temperature and it is oxidized very slowly by potassium permanganate dissolved in acetone.

Methoxybenzalacetone.

The object of the experiments with methoxybenzalacetone was to determine the effect of changing the chemical charac-

ter of an aromatic residue in combination with one of the unsaturated carbon atoms. The methoxyl group has a greater influence than any other substituent that does not interfere with the use of Grignard's reagent, and the measurements of Petrenko-Kritschenko,[1] as well as the experiments of Wieland,[2] show that this extends to the unsaturated side chain. As the following results show, however, the relative amounts of 1,4- and 1,2-addition obtained with *p*-methoxybenzalacetone are almost exactly the same as those obtained with benzalacetone.

Reaction with Ethylmagnesium Bromide: *p-Methoxyphenylhexanone*, $C_2H_5CH(C_6H_4OCH_3)CH_2COCH_3$.—The reaction was carried out exactly like that with benzalacetone and the ketone separated in the same way. It is a mobile liquid boiling at 170° (18 mm.). Sixty grams of unsaturated compound gave 43 grams of ketone.

Analysis:

0.1551 gram substance gave 0.4300 gram CO_2 and 0.1209 gram H_2O.

	Calculated for $C_{13}H_{18}O_2$.	Found.
C	75.72	75.61
H	8.73	8.66

The oxime is a viscous liquid boiling at 195° (18 mm.).

Analysis:

0.1611 gram substance gave 0.4176 gram CO_2 and 0.1285 gram H_2O.

	Calculated for $C_{13}H_{19}O_2N$.	Found.
C	70.58	70.69
H	8.60	8.87

Dibenzalacetone.

Reaction with Ethylmagnesium Bromide: *Benzalphenylhexanone*, $C_6H_5CH:CHCOCH_2CH(C_6H_5)C_2H_5$.—The finely powdered solid ketone was added in small quantities to excess of the reagent. A part of the solid product crystallized from the ethereal solution when the magnesium derivative was poured on ice and acidified. This was removed and the

[1] Ann. Chem. (Liebig), **311**, 167.

[2] *Ibid.*, **329**, 5225.

ethereal solution dried and evaporated. It left an oil that was fractioned under diminished pressure, yielding more of the solid and a relatively small quantity of a colored oil that distilled at 224°–228°. The solid was purified from low-boiling ligroin, from which it separated in long needles melting at 87°.

Analysis:

0.1282 gram substance gave 0.4055 gram CO_2 and 0.0897 gram H_2O.

	Calculated for $C_{19}H_{20}O$.	Found.
C	86.36	86.29
H	7.57	7.71

Benzalphenylhexanone is quite colorless, although unsaturated. It readily combines with bromine and it reduces a solution of potassium permanganate in acetone at the ordinary temperature, the oxidation products being benzoic and β-phenylvaleric acids. The yield is 51 grams from 50 grams of unsaturated ketone—90 per cent of the possible amount.

The nature of the colored oil forming the balance of the product was not definitely established. Although repeatedly distilled under diminished pressure, it was never obtained in perfectly pure condition. The analyses gave results that were too low for a hydrocarbon and too high for any oxygen compound that might be expected. The principal products of oxidation were benzoic acid and a smaller quantity of phenylvaleric acid. The oil is, therefore, probably a mixture of ketone and hydrocarbon.

Benzalphenylhexanonoxime, $C_6H_5CH:CHC(NOH)CH_2CH(C_6H_5)C_2H_5$, was obtained by boiling an alcoholic solution of the ketone with hydroxylamine hydrochloride. It was purified by recrystallization from aqueous alcohol, from which it separates in needles melting at 117°.

Analysis:

0.1404 gram substance gave 0.4211 gram CO_2 and 0.0979 gram H_2O.

	Calculated for $C_{19}H_{21}ON$.	Found.
C	81.72	81.80
H	7.56	7.77

Reaction with Phenylmagnesium Bromide: *Benzaldiphenylbutanone*, $C_6H_5CH:CHCOCH_2CH(C_6H_5)_2$.—Sixty grams of unsaturated ketone were used in the experiment. A part of the product separated in crystalline form when the magnesium derivatives were poured into iced acid. More of this solid was obtained by distilling the filtrate with steam until free from brombenzene and diphenyl, and dissolving the residue in ligroin. The solid was purified by recrystallization from absolute alcohol.

Analysis:

0.2950 gram substance gave 0.9581 gram CO_2 and 0.1727 gram H_2O.

	Calculated for $C_{29}H_{26}O$.	Found.
C	88.61	88.57
H	6.41	6.50

Benzaldiphenylbutanone crystallizes in very pale yellow needles melting at 136°. It is readily soluble in chloroform and acetone, moderately in boiling absolute alcohol and ether, sparingly in cold alcohol and ligroin. It dissolves slowly in cold concentrated sulphuric acid and is precipitated unchanged when water is added to the blood-red solution. The yield was 57 grams, but this is probably less than the amount formed, as some ketone doubtless remained in solution in the residual oil from which no pure substances were obtained.

Benzaldiphenylbutanonoxime, $C_6H_5CH:CHC(CH_2CH(C_6H_5)_2):NOH$, was obtained by boiling an alcoholic solution of the ketone with hydroxylamine hydrochloride and solid sodium carbonate. It crystallizes from alcohol in needles melting at 144°.

Analysis:

0.1120 gram substance gave 0.3460 gram CO_2 and 0.0654 gram H_2O.

	Calculated for $C_{29}H_{27}ON$.	Found.
C	84.40	84.24
H	6.42	6.52

Dibromtriphenylpentanone, $C_6H_5CHBrCHBrCOCH_2CH(C_6H_5)_2$. — Benzaldiphenylbutanone readily combines with one molecule of bromine. Five

grams of the ketone were dissolved in chloroform and treated with bromine in slight excess. The solution was heated to boiling and poured into three times its volume of hot alcohol. The dibromide separated in colorless needles melting at 166°. It is readily soluble in chloroform, sparingly in acetone, alcohol and ether.

Analysis:

0.1606 gram substance gave 0.3432 gram CO_2 and 0.0570 gram H_2O.

	Calculated for $C_{25}H_{30}OBr_2$.	Found.
C	58.47	58.08
H	4.29	4.42

Benzalphenylhexanone.

Reaction with Ethylmagnesium Bromide: *Diphenylnonanone*, $C_2H_5CH(C_6H_5)CH_2COCH_2CH(C_6H_5)C_2H_5$.—The ketone is the only product of the reaction. It separated in solid form when the magnesium derivative was poured into iced acid. The filtrate from the solid, freed from ether and dissolved in acetone, reduced a small quantity of permanganate but no benzoic acid could be detected in the products of oxidation. The ketone was purified from ether-ligroin. It is readily soluble in organic solvents, crystallizes in needles and melts at 56°.

Analysis:

0.1291 gram substance gave 0.4045 gram CO_2 and 0.1045 gram H_2O.

	Calculated for $C_{21}H_{26}O$.	Found.
C	85.71	85.45
H	8.84	8.99

Reaction with Phenylmagnesium Bromide: *Triphenylheptanone*, $(C_6H_5)_2CHCH_2COCH_2CH(C_6H_5)C_2H_5$.—Twenty grams of ketone were used in the experiment. The principal product separated in solid form when the magnesium derivatives were poured into iced acid. The filtrate from the solid was dried, freed from ether, dissolved in acetone and treated with potassium permanganate. Four grams of the oxidizing agent were reduced and 0.6 gram of benzoic acid was extracted from the oxides of manganese. The experiment was repeated

with three times the calculated quantity of reagent and the mixture was boiled for an hour before it was poured on ice, but the product again reduced permanganate and gave 0.55 gram of benzoic acid, indicating the presence of tertiary alcohol or unsaturated hydrocarbon as a result of 1,2-addition.

The solid was purified from absolute alcohol. It is readily soluble in organic solvents and crystallizes in needles melting at 72°. The yield was 23 grams.

Analysis:

0.1404 gram substance gave 0.4520 gram CO_2 and 0.0986 gram H_2O.

	Calculated for $C_{28}H_{28}O$.	Found.
C	87.75	87.79
H	7.63	7.79

Bromtriphenylheptanone, $(C_6H_5)_2CHCHBrCOCH_2CH(C_6H_5)C_2H_5$. — Benzalphenylheptanone was added to phenylmagnesium bromide as before, the resulting magnesium derivative cooled in a freezing mixture and treated with slight excess of dry bromine. The product was purified by crystallization from a mixture of chloroform and alcohol. It crystallizes in needles melting at 153°.

Analysis:

0.1711 gram substance gave 0.4453 gram CO_2 and 0.0926 gram H_2O.

	Calculated for $C_{28}H_{29}BrO$.	Found.
C	71.25	70.91
H	5.95	6.00

The bromketone is readily soluble in ether and chloroform, moderately in boiling absolute alcohol. The bromine is easily eliminated by boiling with alcoholic potassium, but I have not succeeded in getting an unsaturated ketone or any other definite product of the reaction.

Benzaldiphenylbutanone.

Reaction with Ethylmagnesium Bromide.—It was to be expected that the principal product of this reaction would be the same as that obtained by adding phenylmagnesium bromide to benzalphenylhexanone.

I. $(C_6H_5)_2CHCH_2COCH:CHC_6H_5 + C_2H_5MgBr + H_2O = (C_6H_5)_2CHCH_2COCH_2CH(C_6H_5)C_2H_5$;

II. $C_6H_5CH:CHCOCH_2CH(C_6H_5)C_2H_5 + C_6H_5MgBr + H_2O = (C_6H_5)_2CHCH_2COCH_2CH(C_6H_5)C_2H_5$.

It was shown above that about 7 per cent of the product obtained from benzalphenylhexanone consists of an unsaturated compound formed by 1,2-addition. It was of interest, therefore, to determine whether a similar result would be obtained with benzaldiphenylbutanone. The experiment was performed with 20 grams of ketone and the entire product treated with permanganate dissolved in acetone. It reduced less than 0.5 gram of oxidizing agent, and not a trace of benzoic acid was found in the oxidation products. There was, therefore, no 1,2-addition, the sole product being triphenylheptanone. The yield of pure ketone was 24.6 grams.

Reaction with Phenylmagnesium Bromide.—The experiment was performed with 40 grams of unsaturated ketone. Most of the product separated in crystalline form when the magnesium derivative was poured on ice. The filtrate from the solid was freed from ether, dissolved in acetone and treated with permanganate. It reduced 3.8 grams of the oxidizing agent. The salts extracted from the oxides of manganese were acidified and yielded 1.2 grams of a mixture of benzoic and diphenylpropionic acids. This shows that 0.35 per cent of the product consists of unsaturated compounds due to 1,2-addition.

The filtrate from the oxides of manganese was evaporated and the residue distilled with steam. This left a small quantity of solid, which was combined with that which had separated from ether and the whole purified from absolute alcohol. The pure substance melted at 128°. It was identified with the tetraphenylpentanone previously obtained while determining the structure of complex products. The yield was 23.2 grams.

Bromtetraphenylpentanone, $(C_6H_5)_2CHCHBrCOCH_2CH(C_6H_5)_2$.—Bromine reacts with tetraphenylpentanone dissolved in chloroform, but the result is an oily mixture of products. The bromketone is, however,

easily made from the magnesium derivative of tetraphenylpentanol. Dry bromine was added in slight excess to the liquid obtained by adding 30 grams of benzaldiphenylbutanone to phenylmagnesium bromide. A considerable quantity of the product separated during the addition, the remainder when the magnesium derivatives were poured into ice-water. The solid was purified by crystallization from a mixture of chloroform and alcohol.

Analysis:

0.1480 gram substance gave 0.4038 gram CO_2 and 0.0746 gram H_2O.

	Calculated for $C_{29}H_{25}OBr$.	Found.
C	74.20	74.41
H	5.35	5.60

The substance crystallizes in needles melting at 160°. It is readily soluble in chloroform, moderately in ethyl acetate and acetone, sparingly in alcohol and ether. When boiled with alcoholic potassium hydroxide it readily loses bromine but the product is not an unsaturated ketone.

Chloralacetophenone.

Phenyltrichlorbutyrophenone, $CCl_3CH(C_6H_5)CH_2COC_6H_5$. — Chloralacetophenone reacts with phenylmagnesium bromide at the ordinary temperature. The principal product is a saturated ketone melting at 137°. Whether any unsaturated alcohol is formed could not be determined, because the ketone slowly reduces permanganate and gives benzoic acid as one of the products. The yield of pure ketone was 93 per cent of the calculated quantity.

Analysis:

0.2011 gram substance gave 0.4070 gram CO_2 and 0.0757 gram H_2O.

	Calculated for $C_{16}H_{13}OCl_3$.	Found.
C	55.54	55.15
H	4.00	4.13

Benzalacetophenone.

Reaction with Ethylmagnesium Bromide: *β-Phenylvalerophenone*, $C_2H_5CH(C_6H_5)CH_2COC_6H_5$.—Thirty grams of unsat-

urated ketone were used in the experiment. The product reduced 3 grams of potassium permanganate, but only 0.2 gram of benzoic acid was obtained when the oxides of manganese were extracted with boiling water and the solution acidified. This shows that very little of the reduction was due to unsaturated products. The filtrate from the oxides of manganese was evaporated and the residue distilled under diminished pressure. The entire amount distilled within 2°, showing the absence of complex products. The solid distillate was crystallized from absolute alcohol. The yield was 33 grams.

Analysis:

0.1428 gram substance gave 0.4493 gram CO_2 and 0.0990 gram H_2O.

	Calculated for $C_{17}H_{18}O$.	Found.
C	85.71	85.80
H	7.56	7.77

The ketone is readily soluble in organic solvents. It crystallizes in thin needles melting at 63°.

Phenylvalerophenonoxime, $C_2H_5CH(C_6H_5)CH_2C(C_6H_5):NOH$, was obtained by boiling the ketone with an alkaline solution of hydroxylamine and purifying the product from ligroin. It is deposited in needles melting at 87°.

Analysis:

0.1525 gram substance gave 0.4518 gram CO_2 and 0.1059 gram H_2O.

	Calculated for $C_{17}H_{19}ON$.	Found.
C	80.61	80.79
H	7.51	7.71

Reaction with Phenylmagnesium Bromide.—In an earlier paper[1] it was shown that the principal product of this reaction is diphenylpropiophenone. I repeated the experiment in order to determine whether any 1,2-addition product is formed as a result of 1,2-addition to carbonyl. For this purpose the product from 50 grams of unsaturated ketone was dissolved in acetone and treated with potassium permanganate. It reduced 7 grams of the oxidizing agent and gave 1.2 grams

[1] THIS JOURNAL, **33**, 642.

of benzoic acid. This represents approximately 4 per cent of the unsaturated ketone. The filtrate from the oxides of manganese was distilled with steam and the residue crystallized from alcohol. It yielded 58.5 grams of ketone, representing 94 per cent of benzalacetophenone.

Anisalacetophenone.

Reaction with Ethylmagnesium Bromide: *p-Methoxyphenylvalerophenone*, $C_2H_5CH(C_6H_4OCH_3)CH_2COC_6H_5$.—The product obtained from 4.5 grams of ketone reduced 2.2 grams of permanganate and gave 0.35 gram anisic acid. The filtrate from the oxides of manganese was evaporated and the residue recrystallized from methyl alcohol. It separated in thick, lustrous needles, melting at 58°. The yield was 47.5 grams.

Analysis:

0.1633 gram substance gave 0.4910 gram CO_2 and 0.1116 gram H_2O.

	Calculated for $C_{18}H_{20}O_2$.	Found.
C	80.59	80.19
H	7.48	7.59

The oxime was prepared in the usual way and purified by recrystallization from ligroin. It is readily soluble in alcohol and ether, sparingly in ligroin (30°–50°). It separates in prisms melting at 92°.

Analysis:

0.1555 gram substance gave 0.4333 gram CO_2 and 0.1037 gram H_2O.

	Calculated for $C_{18}H_{21}O_2N$.	Found.
C	76.32	75.99
H	7.42	7.41

Reaction with Phenylmagnesium Bromide: *Anisylphenylpropiophenone*, $CH_3OC_6H_4CH(C_6H_5)CH_2COC_6H_5$.—The product from 50 grams of unsaturated ketone reduced 4.8 grams of permanganate, and 1.1 grams of anisic acid were obtained by extracting the oxides of manganese with boiling water. This represents 1.7 per cent of the unsaturated ketone. The filtrate from the oxides of manganese was distilled with steam and the residue crystallized from alcohol.

Analysis:

0.1322 gram substance gave 0.4041 gram CO_2 and 0.0770 gram H_2O.

	Calculated for $C_{23}H_{20}O_2$.	Found.
C	83.54	83.34
H	6.33	6.47

Anisylphenylpropiophenone crystallizes in stout needles melting at 93°. It is readily soluble in ether and acetone, moderately in alcohol, sparingly in ligroin. The yield was 63.5 grams.

Benzalmethylanisyl Ketone.

Reaction with Ethylmagnesium Bromide: *β-Phenylbutylanisyl Ketone*, $C_2H_5CH(C_6H_5)CH_2COC_6H_4OCH_3$.—The product from 30 grams reduced 2.2 grams of permanganate but gave only a trace of benzoic acid, showing that most, if not all, of the reduction was due to impurities introduced with the reagents. The ketone was purified from a mixture of ether and ligroin. It is readily soluble in all organic solvents except ligroin and always crystallizes in long, thin needles melting at 85°. The yield was 32 grams.

Analysis:

0.1601 gram substance gave 0.4726 gram CO_2 and 0.1095 gram H_2O.

	Calculated for $C_{18}H_{20}O_2$.	Found.
C	80.60	80.51
H	7.48	7.59

The *oxime* was made in the usual way and purified from methyl alcohol. It crystallizes in large prisms and melts at 72°.

Analysis:

0.1442 gram substance gave 0.4022 gram CO_2 and 0.0981 gram H_2O.

	Calculated for $C_{18}H_{21}O_2N$.	Found.
C	76.32	76.08
H	7.42	7.62

Reaction with Phenylmagnesium Bromide: *Diphenylethylanisyl Ketone*, $(C_6H_5)_2CHCH_2COC_6H_4OCH_3$.—As benzalmethyl-

anisyl ketone is sparingly soluble in ether it was added to phenylmagnesium bromide in the form of a very fine powder. Most of the product separated in crystals when the resulting magnesium derivatives were poured into iced acid. The solid was removed, the filtrate dried and evaporated, and the residue as well as the crystals dissolved in acetone. This solution reduced 1.8 grams of permanganate, but only a trace of benzoic acid was obtained from the oxidation products. The filtrate from the oxides of manganese was distilled with steam and the residue purified by crystallization from absolute alcohol. The yield was 32 grams of pure ketone from 25 grams of unsaturated compound.

Analysis:

0.1504 gram substance gave 0.4840 gram CO_2 and 0.0898 gram H_2O.

	Calculated for $C_{29}H_{24}O_2$.	Found.
C	83.55	83.28
H	6.33	6.29

Diphenylethylanisyl ketone melts at 118°. It is less soluble than the isomeric anisylphenylpropiophenone and crystallizes much better from all solvents.

Bromdiphenylethylanisyl Ketone.—The ketone reacts readily with bromine dissolved in chloroform. The bromine substitution product was purified by solution in chloroform and precipitation with absolute alcohol. It is readily soluble in chloroform and ethyl acetate, sparingly in acetone and alcohol. The melting point is 144°.

Analysis:

0.1437 gram substance gave 0.3531 gram CO_2 and 0.0637 gram H_2O.

	Calculated for $C_{29}H_{19}O_2Br$.	Found.
C	66.83	67.01
H	4.81	4.93

β-Phenylbenzalmethylanisyl Ketone, $(C_6H_5)_2C:CHCOC_6H_4OCH_3$.—Bromdiphenylethylanisyl ketone was suspended in boiling absolute alcohol and treated with concentrated aqueous potassium hydroxide until the solution remained alkaline after boiling for an hour. The alcohol

was then removed and the residue poured into ice-water. The unsaturated ketone separated as a pale yellow oil, but gradually solidified. The solid was purified from ligroin.

Analysis:

0.1368 gram substance gave 0.4205 gram CO_2 and 0.0725 gram H_2O.

	Calculated for $C_{29}H_{18}O_3$.	Found.
C	84.07	83.83
H	5.73	5.88

Benzalphenylmethylanisyl ketone crystallizes from alcohol in large, pale yellow prisms that gradually lose their brilliant lustre. From ligroin it separates in deep yellow tables that are permanent. It is readily soluble in alcohol, moderately in ether, sparingly in ligroin. Its melting-point is 103°. The yield was excellent—37 grams from 50 grams of the brom-ketone.

α-Brom-β-phenylbenzalmethylanisyl Ketone, $(C_6H_5)_2C:CBrCOC_6H_4OCH_3$, was obtained without difficulty by adding bromine to a hot solution of the unsaturated ketone in chloroform. It is sparingly soluble in alcohol and ether, readily in chloroform. It crystallizes in small needles, melting at 157°.

Analysis:

0.1437 gram substance gave 0.3520 gram CO_2 and 0.0561 gram H_2O.

	Calculated for $C_{29}H_{17}O_2Br$.	Found.
C	67.18	66.84
H	4.32	4.41

In acetone solution the substance slowly reduces permanganate. The only organic products obtained were anisic acid, which was extracted from the oxides of manganese, and benzophenone, which was found in the acetone. These products prove that the bromine is in the side chain as represented.

Benzalacetomesitylene.

Preparation. — Benzalacetomesitylene was made by the Friedel and Crafts reaction. One hundred grams of finely powdered aluminium chloride were added, in small quantities,

to a solution of 96 grams of mesitylene and 160 grams of cinnamyl chloride in 500 grams of carbon bisulphide. The mixture was cooled with running water until all of the aluminium chloride had been added, then exposed to direct sunlight for three hours. The orange-colored liquid was poured on ice and freed from carbon bisulphide by distillation with steam. This left a pasty, yellow residue, which was dissolved in ether and washed thoroughly, first with hydrochloric acid, then with sodium hydroxide until the washings were free from cinnamic acid. The ethereal solution was dried over sodium sulphate, the ether removed and the ketone distilled under diminished pressure. Almost the entire amount distilled between 230°–235° (15 mm.). The distillate—a pale yellow, viscous liquid—solidified in a few days. The solid was recrystallized from ligroin.

Analysis:

0.1530 gram substance gave 0.4830 gram CO_2 and 0.1010 gram H_2O.

	Calculated for $C_{19}H_{18}O$.	Found.
C	86.4	86.1
H	7.2	7.33

Benzalacetomesitylene crystallizes in large, yellow plates that melt at 63°. It is readily soluble in organic solvents and in concentrated sulphuric acid. In a later paper I expect to present a detailed study of this interesting unsaturated ketone. For the purpose of this paper it is sufficient to indicate the relative activity of the carbonyl groups and the ethylene linkage.

The carbonyl group in benzalacetomesitylene is comparatively inactive because neither oxime nor phenylhydrazone is obtained under conditions that usually give these derivatives. This was established by boiling the ketone with an alkaline solution of hydroxylamine for three hours and with an alcoholic solution of phenylhydrazine for six hours. The ethylene linkage, on the other hand, is not affected by the methyl groups in the diortho positions. This is shown by the ease with which the ketone is oxidized to benzoic and mesitylenic

acids and also by the rapidity with which it combines with bromine.

Dibromphenylpropionylmesitylene, $C_6H_5CHBrCHBrCOC_6H_2(CH_3)_3$.—The unsaturated ketone instantaneously decolorized a solution of bromine in carbon bisulphide. The dibromide separated in colorless needles, easily purified by recrystallization from chloroform. It melts, with decomposition, at 122°.

Analysis:

0.0846 gram substance gave 0.1617 gram CO_2 and 0.0310 gram H_2O.

	Calculated for $C_{18}H_{18}OBr_2$.	Found.
C	52.63	52.50
H	4.39	4.10

Reaction with Phenylmagnesium Bromide: *Diphenylpropionylmesitylene*, $(C_6H_5)_2CHCH_2COC_6H_2(CH_3)_3$.—The substances react very readily, the intermediate compound disappearing almost as fast as it is formed. The product reduced a little over 1 gram of permanganate, but as no benzoic acid was found in the oxidation products the reduction must have been due to impurities in the materials that were used. The ketone was recrystallized from absolute alcohol. The yield was 62 grams of pure ketone from 50 grams of unsaturated compound.

Analysis:

0.1044 gram substance gave 0.3365 gram CO_2 and 0.0700 gram H_2O.

	Calculated for $C_{24}H_{24}O$.	Found.
C	87.80	87.91
H	7.32	7.45

Diphenylpropionylmesitylene is readily soluble in acetone and boiling absolute alcohol, moderately in ether, sparingly in ligroin. Like other mesitylene ketones, it forms no oxime when boiled with an alkaline solution of hydroxylamine.

Bromdiphenylpropionylmesitylene, $(C_6H_5)_2CHCHBrCOC_6H_2(CH_3)_3$, was obtained by adding the calculated quantity of bromine to a solution of the ketone in chloroform and warming the liquid until it became colorless.

The substance was purified by crystallization from a mixture of chloroform and alcohol. It is readily soluble in chloroform, moderately in ether, sparingly in absolute alcohol. It crystallizes in needles melting at 172°.

Analysis:

0.1406 gram substance gave 0.3614 gram CO_2 and 0.0731 gram H_2O.

	Calculated for $C_{24}H_{23}OBr$.	Found.
C	70.76	70.40
H	5.65	5.80

Phenylbenzalacetomesitylene, $(C_6H_5)_2CH:CHCOC_6H_2(CH_3)_3$.—A strong solution of 4 grams of potassium hydroxide was added to 24 grams of bromdiphenylpropionylmesitylene suspended in absolute alcohol, and the mixture boiled for an hour. Most of the alcohol was then distilled and the residue poured into ice-water. The precipitated lemon-yellow oil soon solidified. The solid was purified by crystallization—first from alcohol, then from ligroin.

Analysis:

0.1321 gram substance gave 0.4272 gram CO_2 and 0.0832 gram H_2O.

	Calculated for $C_{24}H_{22}O$.	Found.
C	88.34	88.19
H	6.74	7.00

The ketone crystallizes in dark yellow plates melting at 104°. It is readily soluble in organic solvents except low-boiling ligroin. Water precipitates unchanged ketone from its blood-red solution in concentrated sulphuric acid. No oxime was obtained when the ketone was boiled with an alkaline solution of hydroxylamine.

Brombenzalacetophenone, Benzalpropiophenone and Benzaldesoxybenzoin.

It was necessary to repeat previous experiments with these ketones, because no adequate measures had been taken, at the time, to detect small quantities of unsaturated compounds that might be formed by 1,2-addition.

The product obtained from each of these ketones reduced

a small quantity of permanganate, but the reduction was always due to impurities introduced with the material, because no benzoic acid could be detected in the oxidation products. The substituents in the α-position, therefore, interfere with addition to carbonyl.

Dypnone.

Reaction with Ethylmagnesium Bromide: Methylphenylvalerophenone, $C_2H_5C(CH_3)(C_6H_5)CH_2COC_6H_5$.—The reagents were brought together in the usual way, but to make sure of complete reaction the mixture was boiled for an hour before it was decomposed with iced acid. The product was dissolved in acetone and treated with permanganate. Benzoic and acetic acids were obtained by extracting the oxides of manganese with boiling water and acidifying the solution. The filtrate from the oxides of manganese, on evaporation, left an oil that was distilled under diminished pressure and thus separated into acetophenone, boiling at 120° (18 mm.), and methylphenylvalerophenone, boiling at 202° (18 mm.). The yield of the latter was 10 grams from 20 grams of unsaturated compound.

Analysis:

0.1313 gram substance gave 0.4112 gram CO_2 and 0.0945 gram H_2O.

	Calculated for $C_{19}H_{22}O$.	Found.
C	85.71	85.41
H	7.93	7.99

Methylphenylvalerophenonoxime, $C_2H_5CH(CH_3)(C_6H_5)CH_2C(C_6H_5):NOH$, was obtained in the usual way and purified by vacuum distillation. It boils at 222° (15 mm.). At the ordinary temperature it is a horn-like mass, without any tendency to crystallization.

Analysis:

0.1522 gram substance gave 0.4522 gram CO_2 and 0.1109 gram H_2O.

	Calculated for $C_{19}H_{23}ON$.	Found.
C	80.90	81.03
H	7.86	8.09

Reaction with Phenylmagnesium Bromide.—In an earlier paper it was shown that one of the substances formed in this reaction is diphenylbutyrophenone. To determine the nature and amounts of other products, the mixture obtained by decomposing the magnesium derivatives with iced acid was dried, dissolved in acetone and treated with permanganate in the usual way. The filtrate from the oxides of manganese was distilled with steam, the residue dissolved in absolute alcohol and the solution cooled in a freezing mixture. It deposited pure diphenylbutyrophenone. The filtrate from this ketone, when fractioned under diminished pressure, gave benzophenone and a small quantity of diphenylbutyrophenone, making the total yield of the latter 10.1 grams from 20 grams of dypnone.

The oxides of manganese were extracted with water, but only carbon dioxide and a trace of benzoic acid were found in the solution. The steam distillate was fractioned and found to contain a considerable quantity of acetophenone. The products of oxidation were, therefore, benzophenone and acetophenone.

$$CH_3C(C_6H_5):CHC(OH)(C_6H_5)_2 + 4O = (C_6H_5)_2CO + CH_3COC_6H_5 + CO_2 + H_2O.$$

Phenylbenzalacetophenone.

Reaction with Ethylmagnesium Bromide: Diphenylvalerophenone, $C_2H_5C(C_6H_5)_2CH_2COC_6H_5$.—The procedure was the same as that followed in the experiments with dypnone. The principal product is unsaturated: 40 grams of the ketone gave only 8 grams of unoxidizable product. This was purified by distillation. It is a colorless oil boiling at 252° (15 mm.).

Analysis:

0.1262 gram substance gave 0.4055 gram CO_2 and 0.0810 gram H_2O.

	Calculated for $C_{25}H_{26}O$.	Found.
C	87.90	87.54
H	7.00	7.13

Diphenylvalerophenonoxime, $C_2H_5CH(C_6H_5)_2CH_2COC_6H_5$. — The product obtained by boiling the ketone with an alkaline solution of hydroxylamine decomposed when distilled under the lowest pressure available and failed to solidify in a freezing mixture. It was, therefore, thoroughly washed with water, dried at 100° under diminished pressure and extracted with ligroin to remove any unchanged ketone. The colorless residue, which closely resembled the oxime of diphenylbutyrophenone, was analyzed.

0.1600 gram substance gave 0.4941 gram CO_2 and 0.1053 gram H_2O.

	Calculated for $C_{29}H_{29}ON$.	Found.
C	83.89	84.21
H	7.00	7.31

Reaction with Phenylmagnesium Bromide.—This reaction gave no saturated ketone. The only products obtained were the unsaturated alcohol and hydrocarbon, since described by Vorlander and Siebert.[1]

Diphenylbenzalacetophenone.

Preparation.—The substance is easily made by boiling bromtriphenylpropiophenone, suspended in absolute alcohol, with excess of strong potassium hydroxide. As the unsaturated ketone is but very slightly soluble in alcohol it separates during the operation in minute, pale yellow prisms. After boiling for several hours, these were removed, washed with hot water and recrystallized from ethyl acetate. The ketone crystallizes in aggregates of small, pale yellow needles that melt at 153°. It is sparingly soluble in ether and acetone, moderately in chloroform and ethyl acetate. Its solution in concentrated sulphuric acid is blood-red in color.

Analysis:

0.1280 gram substance gave 0.4186 gram CO_2 and 0.0660 gram H_2O.

	Calculated for $C_{27}H_{20}O$.	Found.
C	90.00	89.90
H	5.55	5.72

[1] Ber. d. chem. Ges., **39**, 1024.

The ketone is an exceedingly inert substance, giving almost none of the typical reactions of ketones and of unsaturated compounds.

Reaction with Ethylmagnesium Bromide.—Diphenylbenzalacetophenone reacts with ethylmagnesium bromide in the cold and forms a product that has the same color as the solution of the ketone in concentrated sulphuric acid. If this product is poured into iced acid the entire amount of ketone is regenerated, but if the liquid in which it is partially dissolved is boiled the color slowly disappears and the final result is a colorless magnesium derivative. When this was poured into iced acid it gave only oily products. Every effort to get solid substances failed. The oil was, therefore, dried, dissolved in acetone and treated with permanganate.

The only substance obtained by extracting the oxides of manganese was acetic acid. The filtrate from the oxides was allowed to evaporate slowly. It deposited some solid and a considerable quantity of oil. The solid proved to be diphenylbenzalacetophenone. More of this substance was obtained by dissolving the oil in absolute alcohol and cooling the solution in a freezing mixture, making the total yield 6 grams from 20 grams of ketone. This shows that at least 30 per cent of the product was an unsaturated hydrocarbon that was oxidized as represented by the equation:

$$(C_6H_5)_2C:C(C_6H_5)C(C_6H_5):CHCH_3 + 3O = (C_6H_5)_2C:C(C_6H_5)COC_6H_5 + CH_3COOH.$$

The oil left after removing the unsaturated ketone as completely as possible was washed thoroughly and dried under diminished pressure, but all efforts to get a pure substance from it failed. The results of analysis and the behavior towards ethylmagnesium bromide indicated a saturated ketone formed by 1,4-addition, but as it has not been possible to prove this conclusively the structure must be left in doubt.

Phenylbenzalmesitylene.

The behavior of this ketone is exactly like that of diphenylbenzalacetophenone. With phenylmagnesium bromide it forms a brilliant red double compound that is not changed by pro-

tracted boiling. When this is decomposed with iced acid it regenerates the original ketone. The red product obtained with ethylmagnesium bromide slowly disappears on boiling, but I have not yet succeeded in getting definite compounds from the resulting magnesium derivative.

Benzoylphenylacetylene.

The experiments with benzoylphenylacetylene were begun with the intention of making a comparative study of the behavior of aliphatic and aromatic acetylenic ketones. While the experiments were in progress Mouren and Brachin published a paper on the aliphatic ketones which showed that these react exactly like benzoylphenylacetylene. Work in this direction has, therefore, been discontinued.

The reaction with phenylmagnesium bromide gave an excellent yield of oxytriphenylpropine, which was identified by comparison with a specimen made as directed by Nef.[1] The small quantity of oil left after removing the alcohol was found to be entirely free from ketone, showing that there was no 1,4-addition.

BRYN MAWR COLLEGE,
May, 1907.

Contributions from the Kent Chemical Laboratory of the University of Chicago.

ON THE BEHAVIOR OF VARIOUS ALDEHYDES, KETONES AND ALCOHOLS TOWARDS OXIDIZING AGENTS.

BY W. DENIS.

The work of Nef[2] on dissociation phenomena shown by the monatomic and polyatomic alcohols, the ketones, aldehydes, etc. makes it possible to follow rigorously by experiment the stages through which an oxidation reaction proceeds in the case of a large number of even decidedly complex aliphatic compounds, as has been shown in a striking manner by the recent work of Evans[3] on benzoylcarbinol and the benzilic acid rearrangement.

[1] Ann. Chem. (Liebig), **308**, 282.
[2] *Ibid.*, **318**, 137; **335**, 191.
[3] THIS JOURNAL, **35**, 115.

At the suggestion and under the guidance of Dr. Nef, I have undertaken a study of the behavior of ethyl alcohol, ethyl ether, acetaldehyde, and acetic acid towards oxidizing agents under various conditions. These experiments then logically led me to a detailed study of the behavior of acetone, acetol, pyruvic acid, and aldehyde, as well as of lactic and mesoxalic acids towards oxidizing agents.

In this connection I have also made a careful study of the various reactions shown by ethyl-1,2-diketobutyrate, pyruvic aldehyde and mesoxalic acid.

Quantitative Methods of Work.

The relative amounts of carbonic, formic, oxalic, acetic, lactic, and other acids formed in the various cases were determined quantitatively in the following manner: The alkaline solution was first freed by filtration from insoluble manganese dioxide, silver, mercury, etc., and then treated with the calculated amount of aqueous hydrogen chloride. The carbon dioxide thus set free was driven out of the solution by heating in a flask connected successively with a reversed condenser and with two or three tall cylinders filled with a saturated aqueous solution of barium hydroxide. The hydrogen chloride was added slowly by means of a separatory funnel, and, to insure complete expulsion of the soluble gases, the liquid was finally heated in a bath kept between 110° and 120° for two hours. During all this time a steady stream of air free of carbon dioxide was drawn through the solution. The carbon dioxide was generally absorbed completely in the first cylinder containing the caustic alkali and the precipitated barium carbonate was then filtered off, well washed and dried at 100°.

In those experiments where sodium or potassium hydroxides were used, the amount of carbonic acid present in these reagents was determined by control experiments and was then deducted from the total amount of carbon dioxide obtained in a given experiment. The amount of volatile acids and non-volatile products left in the aqueous solution was now determined as follows:

Water and volatile acids were distilled off at 12 to 20 mm. pressure, heating finally on a boiling water-bath. The salt residue was then thoroughly extracted with ether and the amount of lactic, oxalic, or other non-volatile acids present was determined by the usual methods. The aqueous distillate was made up to a definite volume, and a portion was then titrated with N/10 potassium hydroxide. Only two volatile acids, formic and acetic, were generally present; and in such a case, the amount of formic acid in the solution was always determined quantitatively by its conversion in alkaline solution with N/10 potassium permanganate into carbonate, according to H. C. Jones's method.[1] The amount of acetic acid present could then obviously be determined from the data obtained by the titration with N/10 potassium hydroxide. In those cases where it was found that the aqueous distillate gave a test for hydrogen chloride, this body was removed, when necessary, by treatment with small amounts of silver oxide and subsequent redistillation under reduced pressure.

I. On the Behavior of Ethyl Alcohol, Ethyl Ether and Acetaldehyde towards Potassium Permanganate alone, and in the Presence of Caustic Alkalies.

It has hitherto been assumed that a primary alcohol or its corresponding ether, when treated with oxidizing agents, always goes over quantitatively, with intermediate formation of the aldehyde, into the corresponding fatty acid. The long known conversion of ethyl alcohol by concentrated nitric acid into glyoxal, glyoxylic, and oxalic acids cannot be regarded as an exception to this rule because acetaldehyde, which is first formed, must obviously react at once with the nitrous acid present to give the monoxime of glyoxal according to

$$O = CH - CH_2 - H + \begin{matrix} | \\ O \\ | \end{matrix} - \begin{matrix} | \\ NOH \end{matrix} \rightarrow$$

$$O = CH - CH_2 - N(OH)_2 \rightarrow$$

$$O = CH - CH = NOH + H_2O,$$

[1] THIS JOURNAL, **17**, 537. Cf. Lieben: Monats. Chem., **14**, 146; and Pean de St. Gilles: Ann. Chim. Phys. [3], **55**, 388.

and this compound then gives, by hydrolysis, etc., the products actually obtained.[1] I have found that, when ethyl alcohol, ethyl ether, and acetaldehyde are oxidized in cold aqueous solution with an excess of normal potassium permanganate, acetic acid is the sole reaction product. When, however, potassium hydroxide is present in excess, acetic acid is still the main reaction product, but carbonic and oxalic acids are also formed—in larger amount the greater the concentration of the caustic alkali used. It is certain that these two last-named products cannot possibly originate from a further oxidation of the acetic acid, because special experiments with acetic acid and a great excess of potassium hydroxide prove that no change takes place even in the presence of a large amount of potassium permanganate at 100°. How, then, are we to interpret the formation of carbonic and oxalic acids in the reactions under consideration? The experiments of Nef prove that ethyl alcohol and ethyl ether are dissociated only into water and one or two molecules of ethylidene. The ethylidene molecules present, therefore, take up the hydroxyl groups of the dissociated water or alkali, giving ethylidene dihydroxide, $CH_3CH(OH)_2$, and the atomic hydrogen thus set free is then at once taken up by the permanganate present to give potassium hydroxide and manganese dioxide according to

$$KO-\overset{\overset{O}{\|}}{O=Mn}=O+3H \longrightarrow KOH + MnO_2 + H_2O.$$

It is certain from the work of Wagner, with olefines and permanganate, that if ethylene were present as a product of dissociation of alcohol and ether it must at once give ethyleneglycol or its oxidation products under the conditions employed. Acetic acid is, however, the sole reaction product.

Similarly, ethylidene dihydroxide, $CH_3CH(OH)_2$, is dissociated only into water and ethylidene oxide, $CH_3CH=O$, and hydroxyethylidene, $\begin{matrix}CH_3\\ HO\end{matrix}\!\!>\!C\!<$, respectively; and the last-named substance then at once takes up two hydroxyl

[1] Nef: J. Am. Chem. Soc., **26**, 1574.

groups in the presence of potassium permanganate, giving orthoacetic acid, $CH_3C(OH)_3$, etc. If an aqueous solution of acetaldehyde contained in addition some vinyl alcohol molecules, $CH_2=CHOH$, it is certain that this substance, by uniting with two hydroxyl groups of the dissociated water present, must at once give trihydroxyethane (glycolyl aldehyde), $CH_2OH—CH(OH)_2$, or its further oxidation products. But not a trace of any substance other than acetic acid is obtained when acetaldehyde is oxidized in the presence of aqueous potassium permanganate.

The correctness of these conclusions can, in fact, be tested experimentally, because Nef[1] and McLeod[2] have proved that an aqueous solution of acetaldehyde contains vinyl alcohol molecules as soon as potassium or sodium hydroxides are present in amounts above 0.1 per cent. The vinyl alcohol, which is formed by intramolecular addition from the hydroxyethylidene,

$$HO—C(\diagup\diagdown)—CH_2—H \longrightarrow HOCH=CH_2,$$

is then at once absorbed by unchanged acetaldehyde, with anion rearrangement,[3]

$$\begin{matrix} CH_3CH—O \\ | \quad | \end{matrix} + H—O—CH=CH_2 \longrightarrow CH_3CH(OH)CH_2—CH=O,$$

giving acetaldol, etc. The correctness of all these conclusions is established by the following facts: When an aqueous solution of acetaldehyde is allowed to stand for a long time with freshly precipitated oxide of mercury, no action takes place in the cold; if, however, sodium hydroxide or carbonate is added, the aldehyde present is very rapidly and completely converted, with marked evolution of heat, into white, insoluble, basic mercuric vinylate, $Hg(OCH=CH_2)_2.HgO$, from which, by addition of dilute acids, acetaldehyde can again be regenerated quantitatively. This shows that no vinyl alcohol molecules are present in an aqueous solution of acetaldehyde and that these appear only when sufficient alkali

[1] Ann. Chem. (Liebig), **298**, 316–318.
[2] This Journal, **37**, 25.
[3] Nef: *Ibid.*, **37**, 296, foot-note.

has been added. It is now possible to explain very simply and completely the results obtained when ether, alcohol, or acetaldehyde is treated with aqueous potassium permanganate, alone or in the presence of an excess of caustic alkali. The acetaldehyde, which under all conditions is the first oxidation product of alcohol and ether, must naturally give only acetic acid when the oxidation takes place in the presence of aqueous potassium permanganate, even though a very small amount of potassium hydroxide is formed in the operation according to the equation:

$$KOMnO_3 + 3H \rightarrow KOH + MnO_2 + H_2O.$$

Now the experiments of McLeod show that the concentration of the caustic alkali present must be above a certain definite limit (0.1 per cent) before any molecules of vinyl alcohol appear in the aqueous solution of acetaldehyde. As soon as this happens, these must then obviously be at once removed in the presence of the permanganate to give trihydroxyethane (glycolyl aldehyde), etc. The formation of carbonic and oxalic acids, which is observed in increasing amounts with a greater concentration of caustic alkali, when ethyl alcohol, ethyl ether, or acetaldehyde is oxidized in aqueous solution with permanganate in the presence of potassium hydroxide, must, therefore, be ascribed to the intermediate formation of a simple sugar, a diose, glycolyl aldehyde, which, in turn, owes its origin to an oxidation of the vinyl alcohol molecules as soon as formed.

Glycolyl aldehyde, being dissociated[1] according to

(*a*) $CH_2OH—CHO \rightleftharpoons \rangle CHOH + CH_2O$

and

(*b*) $CH_2OHCH=O \rightleftharpoons \rangle CH.CHO + H_2O,$

is in part (*a*) oxidized, with intermediate formation of two molecules of formic acid to carbon dioxide, and in part (*b*) oxidized (glyoxal, etc.) to oxalic acid as an end-product.

Entirely similar results were obtained in the case of acetone.

[1] Nef: Ann. Chem. (Liebig), 335, 274 and 282.

An aqueous solution of acetone contains the following molecules in dynamic equilibrium:[1]

$$CH_3COCH_3 \rightleftharpoons CH_3COH + \diagup\!\!\diagdown CH_2.$$

When, therefore, this ketone is oxidized in neutral or acid solution with an excess of permanganate, bichromate, etc., acetic and carbonic acids are formed in exactly molecular amounts. An aqueous solution of acetone can consequently contain no trace of enol or β-hydroxypropylene molecules. As soon, however, as a certain definite and very small amount of potassium hydroxide is added to the solution the presence of isoacetone molecules can at once be rigidly established by experimentation in three different ways:

(1) By the quantitative transformation into mercuric β-hydroxypropylene.

(2) By the conversion of acetone into diacetone alcohol, $(CH_3)_2{=}COH{-}CH_2COCH_3$ (addition of the β-hydroxypropylene molecules, with anionic rearrangement, to unchanged acetone).

(3) By the almost quantitative oxidation of the β-hydroxy propylene molecules, with intermediate formation of acetol, trihydroxypropane, $CH_3C(OH)_2CH_2OH$, into equimolecular quantities of carbonic and oxalic acids.

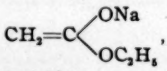
Acetone, as has long been known, does not react in aqueous solution with freshly precipitated and well washed mercuric oxide. As soon, however, as an alkali is added a practically quantitative conversion into snow-white mercuric isoacetone, $(CH_3C(=CH_2){-}O{-})_2Hg$, takes place with marked evolution of heat.

This shows very clearly (1) that an aqueous solution of acetone contains no β-hydroxypropylene molecules; and (2) that such molecules appear in the solution on addition of small amounts of potassium or sodium hydroxide, and that their presence can at once be recognized in the three ways indicated above.

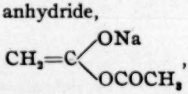
It was now of great interest to determine whether acetic acid, in aqueous solution, contains any isoacetic acid,

[1] Nef: Ann. Chem. (Liebig), **318**, 191 and 227.

$CH_2=C(OH)_2$, molecules, especially in the presence of a great excess of potassium hydroxide, for it may now be considered as practically certain that sodium isoacetic ether,



and sodium isoacetic anhydride,



are the intermediate products formed in the conversion of acetic ether into acetoacetic ether by means of various reagents and in Perkin's reaction, respectively. These are then absorbed with anionic rearrangement[1] by unchanged ethyl acetate or benzaldehyde to give either sodium acetoacetic ether or cinnamic acid.

My experiments show that aqueous solutions of acetic acid, even in the presence of a very great excess of sodium or potassium hydroxide, are unaffected even by prolonged digestion with an excess of potassium permanganate; consequently, no trace of a salt of isoacetic acid can be present, since such a substance would necessarily be immediately oxidized in the cold, with intermediate formation of orthoglycolic acid, $CH_2OH—C(OH)_3$, to oxalic acid. This result shows why condensation reactions with ketones and aldehydes take place with such marvelous ease in the presence of a trace of alkali, whereas those with ethyl acetate, etc., take place with far greater difficulty.

The intermediate formation of an olefine derivative (vinyl alcohol, etc.) is a *conditio sine qua non* in all these condensations, as was first made clear by Nef's work.[2] We must now assume, however, that in these condensations it is *not* the vinyl alcohol derivative that absorbs the ketone, aldehyde, or ethyl acetate, but *vice versa*, *i. e.*, the last-named substances absorb, by carbonyl addition, the dissociated vinyl alcohol derivative, with rearrangement of the anion.[3]

[1] *Loc. cit.*
[2] Ann. Chem. (Liebig), **298**, 315, 319.
[3] Nef: THIS JOURNAL, **37**, 296, foot-note.

Finally, my experiments show very plainly how alcohol, ether, acetone, and acetic acid may be assimilated by plants. Acetaldehyde must obviously be the intermediate product in all cases; this is then transformed, in the presence of enzymes, into vinyl alcohol, which at once takes up two hydroxyl groups, giving glycolyl aldehyde, etc.

Acetaldehyde, Potassium Permanganate, with and without Alkali.—Six grams of freshly distilled acetaldehyde,[1] dissolved in 50 cc. of water, were slowly added, in the cold, and in the course of twenty hours, to 798 cc. of an aqueous solution containing 64 grams of potassium hydroxide (8.5 mols.) and 24.6 grams of potassium permanganate. At the end of this time the pink color of the permanganate had entirely disappeared. On filtering and working up in the usual manner, 8.6 grams barium carbonate, corresponding to 2.02 grams carbon dioxide, and 1.6 grams crystallized oxalic acid (m. p. 103°), were obtained. One hundred and fifty cc. of the aqueous distillate (total volume 3.5 liters) required 5.15 cc. normal potassium hydroxide for neutralization, using phenolphthalein as an indicator. Consequently 6 grams (or 75 per cent of the amount demanded by theory) of acetic acid were present in the aqueous distillate, which was proved to contain no formic acid.

A second experiment was now carried out, in which 10 grams of acetaldehyde, in water, were slowly added within twenty-four hours to an approximately normal solution of potassium permanganate containing 23.9 grams of the salt but no potassium hydroxide. On working up the colorless filtrate in the usual manner and with special care, not a trace of carbonic or oxalic acid could be found. The total volume of the aqueous distillate was 3.5 liters, and 150 cc. of this required 9.44 cc. normal potassium hydroxide for neutralization. Hence the total amount of acetic acid present was 13.2 grams.

Ethyl Alcohol, Permanganate, Etc.—Six and two-tenths grams of absolute alcohol, in 50 cc. water, were slowly added (within twenty-two hours) to 1100 cc. of an aqueous solution containing 33 grams of potassium permanganate and 60 grams

[1] McLeod: THIS JOURNAL, **37**, 28.

(7 mols.) of potassium hydroxide. Complete reduction of the permanganate took place in the cold. Six and four-tenths grams of barium carbonate, which is equivalent to 1.5 grams of carbon dioxide, and 1.4 grams of crystallized oxalic acid were obtained. One hundred and fifty cc. of the aqueous distillate (volume, 3.5 liters) required 46.80 cc. N/10 potassium hydroxide for neutralization. The amount of acetic acid present was, therefore, 6.4 grams. Fournier has very recently shown[1] that only 50 per cent of the theoretical amount of acetic acid is formed when ethyl alcohol is oxidized by permanganate in the presence of a large excess of potassium hydroxide. He did not ascertain the nature of the other products formed, but proved that entirely analogous results are obtained with other primary alcohols, such as propyl, isobutyl alcohol, etc. Hammelmeyer[2] and Nef[3] have made entirely similar observations in the case of the spontaneous oxidation of various primary sodium alcoholates in dry air or oxygen, and Dr. Nef informs me that he has never been satisfied with the explanation formerly given by him[4] to account for the presence of large amounts of carbonic, formic and oxalic acids which were observed in addition to the normal oxidation product, *i. e.*, the corresponding fatty acid. These results are now self-evident, since the aldehyde,

$$C_nH_{2n+1}CH=O,$$

first formed in the oxidation must, of necessity, in the presence of the large amount of unchanged sodium alcoholate, be converted into the vinyl alcohol derivative,

$$C_{n'}H_{2n'+1}CH=CHONa \quad (n=n'+1);$$

and this must then, by absorption of two hydroxyl groups, give at once the aldose,

$$C_{n'}H_{2n'+1}CHOH—CH(OH)_2.$$

The atomic hydrogen thus simultaneously set free is taken up by the active molecular oxygen present to give hydrogen

[1] Compt. rend., **144**, 331–333.
[2] Monats. Chem., **18**, 151.
[3] Ann. Chem. (Liebig), **318**, 177.
[4] *Ibid.*, **318**, 179.

peroxide, etc. The aldose or sugar formed is thereupon converted, by further oxidation, into formic, carbonic, oxalic, and other acids, as will be shown in an article by Nef on the oxidation of sugars, soon to be published in Liebig's *Annalen der Chemie.*

In a second experiment, where 1100 cc. of a solution containing 33 grams of potassium permanganate, but no potassium hydroxide, was used, it was found necessary to add 10 grams of absolute alcohol during a period of forty-eight hours before complete decolorization took place in the cold. On working up the reaction products as usual, no trace of carbon dioxide or of oxalic acid could be found: 150 cc. of the aqueous distillate (total volume 3 liters) required 10.30 cc. normal potassium hydroxide for neutralization. Hence, 12.7 grams of acetic acid were present.

Ethyl Ether, Potassium Permanganate, Etc.—The oxidation of ether by potassium permanganate takes place far more slowly than does that of alcohol, since the percentage of ethylidene dissociation in the former case cannot be increased by the presence of potassium hydroxide, whereas in the case of alcohol this can be increased enormously because of the formation of a salt.[1] Nine grams of absolute ether were gradually added in the course of three days to an aqueous solution (volume about 2.3 liters) containing 70.8 grams potassium permanganate and 37.8 grams (5.5 mols.) potassium hydroxide. The mixture was then heated for five hours under a reversed condenser in a bath kept between 45° and 50°.

Four and one-tenth grams of barium carbonate, corresponding to 1.8 grams carbon dioxide, and 2.24 grams crystallized oxalic acid were obtained on proceeding in the usual manner. One hundred cc. of the aqueous distillate (total volume, 4 liters) required 10.08 cc. N/10 potassium hydroxide for neutralization. Hence a total of 10.8 grams of acetic acid was present.

In a second experiment, 1950 cc. of an aqueous solution, containing 62.4 grams of potassium permanganate, were used and 11 grams of ether were added within three days. The mixture was then heated for sixteen hours in a bath kept at

[1] Nef: Ann. Chem. (Liebig), **318**, 138.

45°–50°. Only 0.4 gram of barium carbonate and no trace of oxalic acid was obtained. Fifty cc. of the aqueous distillate (volume, 4.5 liters) required 31.19 cc. N/10 potassium hydroxide for neutralization. Therefore, the amount of acetic acid present was 16.79 grams.

Acetic Acid, Permanganate, Etc.—One gram of potassium acetate in 10 cc. water was digested under a reflux condenser with 50 cc. normal potassium permanganate for one and a half hours in an oil bath kept between 100° and 110°, and then for three hours longer at 115°–120°, but only traces of reduction to manganese dioxide could be noticed, which was probably due to a slight decomposition of the permanganate itself. Entirely analogous results were obtained when the aqueous solution contained, in addition, 4.7 grams (10 mols.) of potassium hydroxide.

II. Acetone, Permanganate, Etc.

As is well known, acetone, when oxidized in acid solutions in the presence of such reagents as potassium bichromate, permanganate, etc., is invariably converted into equimolecular amounts of carbon dioxide and acetic acid.[1] It has, however, recently been shown by Cochenhausen[2] that acetone, when oxidized with an excess of permanganate in strongly alkaline solutions containing 42 molecules of potassium hydroxide for every molecule of acetone, gives practically only molecular amounts of oxalic and carbonic acids. My own experiments show that when acetone is oxidized in alkaline media in the presence of permanganate, acetic as well as carbonic and oxalic acids are formed, and that the relative amount of the last-named acid increases with the concentration of potassium hydroxide employed. Furthermore, my experiments with acetol, lactic, pyruvic, and mesoxalic acids prove that the formation of oxalic acid from acetone is due to the successive intermediate formation of acetol, pyruvic and mesoxalic acids. The acetol is obviously obtained from the oxidation of the isoacetone molecules, which are present in an alkaline solution of acetone, as shown above.

[1] Dumas, Stas, Gottlieb: Ann. Chem. (Liebig), **32**, 130; Hercz: *Ibid.*, **165**, 257.
[2] J. prakt. Chem. [2], **58**, 454.

Five and four-tenths grams of acetone, in 100 cc. water, were slowly added to 1816 cc. of a solution containing 57.2 grams potassium permanganate and 30 grams (5 mols.) of potassium hydroxide. The decolorization of the permanganate was complete after two days' standing in the cold. The amount of carbon dioxide formed was not determined, but 7.1 grams of crystallized oxalic acid, or 58 per cent of the amount demanded by theory, were obtained; in addition, 2.9 grams (31 per cent of theory) of potassium acetate were obtained on neutralizing the aqueous distillate with potassium hydroxide, evaporating and extracting the salt residue with absolute alcohol.

In a second experiment, in which 5.7 grams acetone and 2971 cc. of a solution containing 47.1 grams of potassium permanganate and 4.8 grams (1 mol.) of potassium hydroxide were allowed to stand in the cold overnight, and the mixture then heated for one hour under a reflux condenser, in a bath kept at 60°, I obtained 2.1 grams of oxalic acid (17 per cent of theory) melting at 103° and 5 grams of potassium acetate, or 51 per cent of the amount demanded by theory. A portion of the latter substance was converted by double decomposition into silver acetate and analyzed.

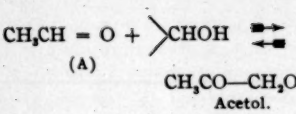
0.4490 gram substance gave, on ignition, 0.2894 gram Ag.

	Calculated for $C_2H_3O_2Ag$.	Found.
Ag	64.5	64.67

In a third experiment, in which 10 grams of acetone and 2250 cc. of a solution containing 72 grams of potassium permanganate, but no potassium hydroxide, were used, the mixture being heated under a reversed condenser for 22 hours, in a bath kept at 50°–55°, I obtained 33 grams of barium carbonate, corresponding to 7.4 grams of carbon dioxide and only 0.3 gram of oxalic acid. Fifty cc. of the aqueous distillate (total volume, 4 liters) required 21.21 cc. N/10 potassium hydroxide for neutralization. Hence the amount of acetic acid present was 10.18 grams.

Acetol, Permanganate, Etc.—An aqueous solution of acetol contains the following molecules[1] in dynamic equilibrium:

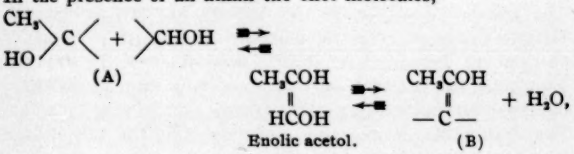
[1] Nef: Ann. Chem. (Liebig), **335**, 269–279.



$$CH_3CH=O + \rangle CHOH \rightleftharpoons CH_3CO{-}CH_2OH \rightleftharpoons CH_3CO.CH + H_2O.$$

(A) Acetol. (B)

In the presence of an alkali the enol molecules,



(A) Enolic acetol. (B)

must also be present.[1] The experiments with permanganate prove that, when acetol is oxidized in the absence of an alkali, no trace of oxalic acid but molecular quantities of acetic and carbonic acids are obtained. In the presence of caustic alkali, however, the amount of acetic acid decreases and that of oxalic acid increases in proportion to the amount of caustic potash added, so that finally almost no acetic acid is formed. This can only mean (1) that without alkali the main reaction consists in the burning of the unsaturated (A) molecules to acetic and carbonic (with intermediate formation of formic) acids; (2) that in the presence of the alkaline hydroxide, which must necessarily increase, through salt-formation,[2] the percentage of dissociation according to (B), the main reaction is conversion of the unsaturated (B) molecules into pyruvic aldehyde.

In order to determine through what stages the transformation of the pyruvic aldehyde proceeds, under the conditions employed, into equal molecules of oxalic and carbonic acid, it was now obviously necessary to try corresponding experiments with pyruvic, lactic and mesoxalic acids.

Experiments with permanganate and pyruvic aldehyde itself have not yet been carried out because I did not succeed in working out a method for obtaining large quantities of this substance until all my other work was practically completed. It is certain, however, from the data obtained that pyruvic, hydroxypyruvic, and mesoxalic acid are successive

[1] Evans: THIS JOURNAL, **35**, 136–142.
[2] Nef: Ann. Chem. (Liebig), **335**, 275.

intermediate products in the transformation of pyruvic aldehyde into oxalic and carbonic acid under the given conditions; the only point in doubt is whether the pyruvic acid is formed (1) through direct oxidation of the aldehyde group, or (2) through an intermediate formation of *d-l*-lactic acid (by the benzilic acid rearrangement[1]) or whether both reactions, (1) and (2), take place simultaneously.

Six and fifty-two hundredths grams of acetol in 30 cc. water were slowly poured into 1400 cc. of a solution containing 42.6 grams potassium permanganate and 37 grams (7.5 mols.) of potassium hydroxide. Vigorous cooling with running water was at first necessary, as oxidation took place with great rapidity and much evolution of heat. On proceeding as usual, after two days' standing, 18.8 grams of barium carbonate, which is equivalent to 3.86 grams of carbon dioxide, and 5.5 grams (50 per cent of the amount demanded by the theory) of crystallized oxalic acid were obtained. Five hundred cc. of the aqueous distillate (total volume, 2.55 liters) required 56.7 cc. N/10 sodium hydroxide for neutralization. Hence 1.74 grams (34 per cent of theory) of acetic acid were present.

A second experiment, with 6.6 grams of acetol and 1221 cc. of a solution containing 36.9 grams of potassium permanganate and 14.9 grams (3 mols.) of potassium hydroxide, gave 3.3 grams carbon dioxide, from 15.4 grams of barium carbonate, and 2.7 grams oxalic acid. The amount of acetic acid present was not determined.

In a third experiment, 6 grams of acetol and 880 cc. of a solution containing 25.6 grams potassium permanganate, but no potassium hydroxide, were used. After four days' standing, 2.7 grams of carbon dioxide (12.3 grams barium carbonate), 4.14 grams of acetic acid, but no trace of oxalic acid, were obtained as reaction-products.

d-l-Lactic Acid, Permanganate, Etc.—Beilstein has shown[2] that calcium lactate, when oxidized with an insufficient amount of potassium permanganate, gives a fair amount of pyruvic

[1] Nef: Ann. Chem. (Liebig), **298**, 372; **335**, 272. Evans: This Journal, **35**, 116–119.

[2] Ber. d. chem. Ges., **17**, 840.

acid. The experiments of Ulzer and Seidel[1] show that lactic acid can be titrated in warm alkaline solution with potassium permanganate, and that oxalic and carbonic acids are formed in molecular amounts according to

$$C_3H_6O_3 + 5O \rightarrow C_2O_4H_2 + CO_2 + 2H_2O.$$

I have repeatedly confirmed these observations of Ulzer and Seidel by titrating lactic acid with N/10 potassium permanganate in the presence of an excess of sodium hydroxide or carbonate at a temperature of 70°, and on titrating subsequently in acid solution, with N/5 oxalic acid, etc., I always found that exactly one molecule of oxalic acid must have been formed in the first stage of the oxidation process. It is obvious that pyruvic acid must be an intermediate product in the transformation of lactic acid under discussion;[2] this is, however, further oxidized because enol molecules of pyruvic acid must, of necessity, be present in the alkaline solution, and these at once take up the hydroxyl groups

$$\begin{array}{l} CH_2 \\ \| \\ COOH.COH \end{array} + 2(HO) \rightarrow \begin{array}{l} CH_2OH \\ | \\ COOH.C(OH)_2, \end{array}$$

giving first hydroxypyruvic acid, which is then oxidized to the ketone aldehyde acid, COOH—CO—CH=O. Mesoxalic acid may then be obtained from this substance (1) by direct oxidation of the aldehyde group; (2) by an intermediate transformation into tartronic acid, COOH—CHOH—COOH, by the benzilic acid rearrangement.

Finally, mesoxalic acid, being dissociated according to

$$COOH—CO—COOH \rightleftharpoons COOH—COOH + \diagup\!\!\!\!\diagdown C=O,$$

must at once give carbon dioxide and oxalic acid under the conditions employed. It is also clear that in case an interference with the benzilic acid rearrangement of CHO—CO—COOH takes place because of the presence of the permanganate,[3] a very small portion of the oxalic and carbonic acids

[1] Monats. Chem., **18**, 138.
[2] Nef: Ann. Chem. (Liebig), **335**, 296–300.
[3] Evans: This Journal, **38**, 118–119.

obtained as end-products must come from the oxidation of the dissociation-products of this aldehyde acid,

$$O=CH—CO—COOH \rightleftharpoons O=CH—COOH + \rangle CO.$$

Lactic acid, 11.1 grams of 87.1 per cent acid, in 50 cc. water, was added to a solution of 57 grams of potassium permanganate and 54.6 grams (9 mols.) potassium hydroxide in 1.1 liters water. Reduction to manganese dioxide took place at once in the cold, and after two days' standing the mixture was heated for two hours in a bath kept at 60°. The amount of carbon dioxide formed was not determined, but 12.6 grams of crystallized oxalic acid, which is 94 per cent of the amount demanded by theory, were obtained in the usual manner.

Finally, the following volumetric data obtained with lactic acid and alkaline permanganate are of interest:

I. 0.1507 gram lactic acid and 1.25 grams sodium hydroxide, in 25 cc. water, required a total of 268.80 cc. N/10 $KMnO_4$ on titrating first in the cold and then, finally, at 60°. On addition of an excess of sulphuric acid a total of 36.06 cc. N/5 oxalic acid was found necessary for the removal of the manganese dioxide. Hence 4.84 atoms oxygen were used up in the first stage of the oxidation process.

II. 0.1765 gram lactic acid, 3 grams dry sodium carbonate and 25 cc. water required a total of 308.09 cc. N/10 $KMnO_4$ for complete oxidation at 65°, *i. e.*, 4.87 atoms oxygen (theory 5 atoms). On addition of sulphuric acid in excess a total of 38.01 cc. N/5 oxalic acid was found necessary to remove the manganese dioxide.

Pyruvic Acid, Permanganate, Etc.—The correctness of the conclusion that pyruvic acid is the intermediate product in the oxidation of acetone, acetol, pyruvic aldehyde and lactic acid in alkaline solution by permanganate is shown by the fact that it is converted under similar conditions, almost quantitatively, into molecular amounts of carbon dioxide and oxalic acid. The pyruvic acid used was freshly prepared and a known weight was then at once dissolved in water and used for various experiments. Two grams of this acid, in 25 cc. water, were added in the cold to 454.8 cc. of a solution

containing 7.186 grams potassium permanganate and 2.8 grams potassium hydroxide. The mixture was heated, after one and a half hours' standing, for forty-five minutes in a bath at 55°–60°. The amount of carbon dioxide formed was not determined, but 2.3 grams of crystallized oxalic acid, melting point 103°, which is 82 per cent of the amount demanded by theory, were obtained.

The following volumetric experiments show that pyruvic acid, when titrated with permanganate in an aqueous solution containing an excess of sodium hydroxide or carbonate, uses up only 3.49 to 3.56 atoms of oxygen, instead of 4 atoms, as demanded by theory, for each molecule of pyruvic acid taken. This is the result even where especial precautions are taken to prevent any condensation of the pyruvic acid at every stage of the operation.

I. 0.1982 gram substance, 5 grams dry sodium carbonate and 300 cc. water required a total of 262.14 cc. N/10 $KMnO_4$ (at 60°). On acidifying with sulphuric acid, etc., a total of 32.27 cc. N/5 oxalic acid was necessary for the removal of the manganese dioxide.

II. 0.2846 gram substance, 3.1 grams potassium hydrate and 300 cc. water required a total of 384.15 cc. N/10 $KMnO_4$ (at 60°). On acidifying with sulphuric acid, etc., a total of 47.82 cc. N/5 oxalic acid was found necessary to remove the manganese dioxide.

Mesoxalic Acid, Permanganate, Etc.—The experiments of Baeyer[1] show that alkaline solutions containing mesoxalic acid are transformed by permanganate into carbonic and oxalic acids. I have confirmed these observations with a preparation of pure mesoxalic acid, melting at 121°, and made according to the directions of Curtiss.[2] On titration in alkaline solution with N/10 potassium permanganate, finally at 60°, it was found that exactly one atom of oxygen is taken up for every molecule of acid used. Furthermore, titration of the acidified solution in the usual manner shows that exactly one molecule of oxalic acid must have been formed in the reaction, as is evident from the following data:

[1] Ann. Chem. (Liebig), 181, 298.
[2] This Journal, 35, 478.

I. 0.1999 gram substance, 25 cc. water and 25 cc. of a 10 per cent solution of sodium carbonate required a total of 48.7 cc. N/10 $KMnO_4$. On adding sulphuric acid, etc., a further addition of 9.09 cc. N/10 $KMnO_4$ was required to remove the oxalic acid still present.

II. 0.1715 gram substance, 20 cc. water and 20 cc. of a 30 per cent solution of sodium carbonate required a total of 41.63 cc. N/10 $KMnO_4$. On adding sulphuric acid, etc., a further addition of 8.35 cc. N/10 $KMnO_4$ was required to oxidize the oxalic acid still present.

III. On the Behavior of Acetol and Pyruvic Aldehyde towards Various Oxidizing Agents.[1]

Acetol, Silver Oxide, Etc.—Acetol, when treated with silver oxide alone or in the presence of potassium hydroxide, is converted quantitatively into equimolecular amounts of acetic and formic acid. This shows that only those molecules of acetol which are dissociated according to

$$CH_3COCH_2OH \rightleftharpoons CH_3CHO + >CHOH$$

and

$$CH_3COH{=}CHOH \rightleftharpoons CH_3(OH)C< + >CHOH$$

are oxidized. Special experiments with aqueous formic acid and silver oxide prove that no trace of carbon dioxide is formed on long standing in the cold.

Five grams acetol in 20 cc. water were added slowly and with continual cooling to a mixture containing 8.2 grams (3 mols.) sodium hydroxide, about 500 cc. water and 3 molecules of freshly precipitated and well-washed silver oxide (from 71 grams silver nitrate). Reduction to silver took place almost instantaneously and after six hours' standing the mixture was worked up as usual. Twenty-seven grams of silver were obtained, but no trace of carbon dioxide or of lactic acid could be detected. Fifty cc. of the aqueous distillate (total volume, 2 liters) required 27.75 cc. N/10 permanganate for oxidation; hence the amount of formic acid present was 2.6 grams. One hundred cc. of the distillate required 6.23 cc. normal sodium hydroxide for neutraliza-

[1] Nef: Ann. Chem. (Liebig), **335**, 269. Kling: Ann. Chim. Phys. [8], **8**, 529.

tion. Therefore, the amount of acetic acid formed in the oxidation was 3.8 grams.

In a second experiment, in which 6 grams of acetol, 4 molecules of freshly precipitated and well washed silver oxide (from 110 grams silver nitrate) and about 500 cc. water (but no caustic alkali) were used, the mixture stood at ordinary temperature for two weeks. No trace of carbon dioxide was observed. On decomposing the silver salts with hydrogen sulphide, etc., the aqueous distillate, free from hydrogen sulphide and acetol, was found by the customary methods to contain 1.7 grams formic and 2.4 grams acetic acid.

Acetol, Mercuric Oxide, Etc.—In marked contrast to these results with silver oxide are the corresponding experiments with acetol and oxide of mercury. An aqueous solution of acetol, when mixed with an emulsion containing freshly precipitated and very carefully washed oxide of mercury, remains unchanged even after standing for weeks at ordinary temperatures (cf. corresponding experiments of Nef and of Kling, *loc. cit.*); and no action takes place even on prolonged heating in a bath kept between 100° and 120°. As soon, however, as a caustic alkali is added, reduction to mercury takes place at once in the cold, but the chief product then formed is racemic-lactic acid, besides small quantities of formic and acetic acid. No trace of carbon dioxide could be detected, although this was looked for with special care in two different experiments.

Ten and eight-tenths grams of acetol, in 50 cc. water, were added slowly to a mixture containing 1.25 molecules of oxide of mercury (from 49.9 grams mercuric chloride), 8.8 grams sodium hydroxide, and about 1 liter of water. Immediate reduction to mercury took place, and after standing for four hours, filtering, etc., 10.4 grams of crystallized zinc lactate, corresponding to 6.365 grams lactic acid, were obtained. The aqueous distillate contained unchanged acetol, but required in all only 0.9 gram sodium hydroxide for neutralization. Consequently, only a small amount of fatty acids could be present. The zinc lactate obtained gave the following analytical results:

I. 4.6288 grams air-dry salt lost, on drying for seven hours, at 100°, 0.8414 gram H_2O.

II. 0.5990 gram anhydrous salt gave, on ignition, 0.2002 gram ZnO.

	Calculated for $(C_3H_5O_3)_2Zn.3H_2O$.	Found.
H_2O	18.16	18.17
Zn	26.89	26.88

A second experiment, in which 6 grams acetol, 3 molecules of mercuric oxide, and 9.7 grams of sodium hydroxide were used, and the mixture was allowed to stand overnight, gave 6.5 grams of zinc lactate. One hundred and fifty cc. of the aqueous distillate (total volume, 3 liters) required 17.35 cc. N/20 sodium hydroxide for neutralization. Hence only 0.693 gram of sodium hydrate are required for the total distillate. Another 150 cc. of the distillate took 18.74 cc. N/10 permanganate for oxidation, from which the total amount of formic acid present is calculated as 0.8 gram, corresponding to 0.693 gram sodium hydroxide. It is very probable, however, that a portion of the very small amount of volatile acid present consisted of acetic acid, and that the results of the titration with permanganate were high because of the presence of a small amount of neutral oxidizable material.

The behavior of acetol towards alkaline solutions containing suspended oxide of mercury, which is so surprisingly different from the results obtained when silver oxide is used in its stead, shows that in this instance only an oxidation of the acetol molecules which are dissociated according to

$$CH_3COCH_2OH \rightleftharpoons CH_3COCH< + H_2O$$

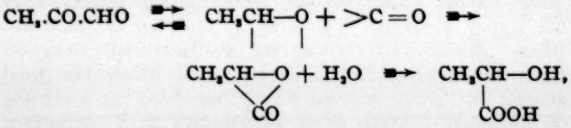
and

$$CH_3COH=CHOH \rightleftharpoons CH_3C(OH)=C< + H_2O$$

takes place; and that, therefore, pyruvic aldehyde must be the primary oxidation product, which then at once undergoes the benzoic acid rearrangement, giving racemic-lactic acid.

On further consideration, this marked difference in the behavior of acetol in the two cases is not so surprising, for oxide of mercury does not react with acet- or formaldehyde in the

absence of alkalies, whereas with silver oxide a rapid oxidation, with deposition of silver, takes place, even in very dilute aqueous solutions. Furthermore, the oxides of silver and mercury, in the presence of alkalies, act in a totally different manner towards acetaldehyde. One other point in the results with acetol, oxide of mercury and alkalies deserves special emphasis. Evans has shown that the transformation of benzoylformaldehyde into racemic-mandelic acid by caustic alkalies is entirely prevented by the presence of either oxide of silver or mercury.[1] We have, therefore, with pyruvic aldehyde, a case where the speed of the benzilic acid rearrangement, according to



is so rapid that no oxidation of the dissociated products of this compound, carbonic oxide and acetaldehyde, can take place. Entirely similar results were obtained (see below) with 1,2-diketobutyric ether and alkalies in the presence of the oxides of silver or mercury; and since Evans has shown[2] that the benzilic acid rearrangement of benzoylformaldehyde with alkaline hydroxides takes place to the extent of 50 per cent, even in the presence of potassium permanganate, it is exceedingly probable that the transformation of pyruvic aldehyde, as well as of mesoxaldehydic acid, HCO.CO.COOH, by caustic alkalies, through a benzilic acid rearrangement, into lactic and tartronic acids cannot be appreciably disturbed when permanganate is also present. I, therefore, consider it in the highest degree probable that racemic-lactic and tartronic acids are the intermediate products formed in the oxidation of acetone, acetol, etc. with permanganate and caustic alkalies, a reaction which has already been discussed at some length in the first part of this paper.

[1] This Journal, **38**, 119.

[2] *Loc. cit.*

Pyruvic Aldehyde and Its Reactions.

It is evident from the work of Nef and Evans that pyruvic aldehyde must be the intermediate product in the conversion of acetol or acetylcarbinol into racemic-lactic acid. This substance has since been obtained in small quantity in the polymeric form by Harries and Türk.[1] It may now be prepared in quantity with the greatest ease from acetol and copper acetate[2] as follows: One hundred and sixty-two grams of very finely powdered copper acetate are mixed with a solution containing 30 grams of acetol and 220 cc. water. The mixture is shaken frequently and allowed to stand at ordinary temperatures for three to four weeks. On filtering in the cold and boiling out the insoluble residue with water, containing small amounts of acetic acid, 42 grams of insoluble cuprous oxide were regularly obtained. Water and acetic acid are now removed as much as possible from the original cold aqueous filtrate by fractionation at 11 mm. pressure, from a bath kept between 35° and 40°. A small amount of methylglyoxal is carried over with the distillate during the operation and is, therefore, lost. The greenish, semi-solid mass left in the distilling flask gave, on thorough extraction with ether, 18.7 grams of a mobile, strong-smelling, green liquid, which is slightly volatile even with ether vapor. It still contains much acetic acid, which is best removed by dissolving in an equal volume of water, and then treating with small amounts of powdered calcium carbonate. After standing for twenty-four hours, the water is distilled off at reduced pressure as before and the residue then well extracted with ether. I obtained thus, in one experiment from 30 grams acetol 9.9 grams of crude polymeric pyruvic aldehyde, which, however, still contained, as shown by titration with N/10 sodium hydroxide, 11 per cent of acetic acid. This product was an extremely viscous, yellow gum, easily soluble, but with slight turbidity, in cold water. The aqueous as well as the ethereal solutions are colored yellowish-green and possess a marked odor, very much like that of diacetyl and strikingly like that

[1] Ber. d. chem. Ges., **38**, 1630.
[2] Nef: Ann. Chem. (Liebig), **335**, 279.

noticed in breweries. In a second experiment with 16 grams acetol, I obtained 5.4 grams of polymeric methylglyoxal as a yellow, brittle, amorphous solid, quite soluble in water and neutral to litmus. It is evident from the recent work of Harries and Temme[1] on glyoxal, that monomolecular methylglyoxal must be a powerful-smelling, yellowish-green liquid, boiling at about 70° at ordinary pressure, and that this substance can probably now be obtained in large amounts by the depolymerization of polymeric pyruvic aldehyde by means of phosphorus pentoxide. I have, as yet, carried out no experiments with this end in view, but have simply been content to prove that my polymeric pyruvic aldehyde gives, in aqueous solution, all the reactions of the monomolecular product.

Thus, 0.4 gram in 5 cc. water gave, on treatment in the cold with 2 grams phenylhydrazine dissolved in 2 cc. 50 per cent acetic acid, 1.3 grams of crude diphenylhydrazone melting at 136°, or, after one crystallization from benzene, at 144°. Another portion, 0.9 gram, of polymeric methylglyoxal in 10 cc. water gave, on treatment with semicarbazide (from 3.4 grams of the hydrochloride, potassium acetate, etc.), 1.3 grams of the disemicarbazone, described by Harries and Türk, in the form of white, microscopic crystals melting at 258° and soluble in about 1,000 parts of boiling water.

An aqueous solution of polymeric methylglyoxal is neutral to litmus, but reduces Fehling's solution in the cold. On heating to 100° (or even to 65°, see below under diketobutyric ether), a slow and incomplete transformation into lactic acid takes place. Thus I obtained 0.3 gram crystallized zinc lactate from 0.9 gram of gum after heating forty-two hours at 100° with 10 cc. water.

Another portion of gum, 0.89 gram in 10 cc. water, gave, on treatment with an aqueous solution containing 4 molecules of potassium hydroxide, and after standing for 2 days in the cold, 0.95 gram crystallized zinc lactate.

A preliminary quantitative experiment, with 2.7 grams polymeric methylglyoxal, much water, 6.4 grams sodium

[1] Ber. d. chem. Ges., **40**, 167.

hydroxide and 3 molecules of freshly precipitated oxide of silver, gave 9.1 grams silver, 0.46 gram carbon dioxide and 0.5 gram zinc lactate.

A second experiment, with 4.27 grams gum, water, 9.3 grams sodium hydroxide and 2.5 molecules silver oxide, gave 13.8 grams silver, 0.83 gram carbon dioxide and 0.95 gram zinc lactate. And, finally, a third experiment, with 1.98 grams gum, 200 cc. water, 4.4 grams sodium hydroxide and 2 molecules of mercuric oxide, gave 0.24 gram carbon dioxide and 1.3 grams zinc lactate. These experiments show conclusively that the benzilic acid rearrangement in the case of methylglyoxal is practically not affected by the presence of oxide of mercury or silver, results which are in harmony with those obtained with acetol, alkali and oxide of mercury described above.

Pyruvic Acid, Silver Oxide, Etc.—Beilstein has shown[1] that aqueous solutions containing pyruvic acid are converted by means of silver oxide, quantitatively, at 100°, into carbon dioxide and acetate of silver. I have found that this transformation takes place smoothly in the cold, even in the presence of an excess of sodium hydroxide. A quantitative experiment, carried out with 4 grams pyruvic acid, 200 cc. water, 7.2 grams sodium hydroxide, and 2 molecules of silver oxide (from 31 grams silver nitrate), gave, after standing for two days in the cold, 8.5 grams silver, 1.75 grams carbon dioxide, and 2 grams of acetic acid.

Similarly, an experiment with 4 grams pyruvic acid, about 250 cc. water, and 2.5 molecules of silver oxide (from 37 grams silver nitrate) gave, after standing for twenty-four hours at ordinary temperatures, 9.2 grams silver and 2.3 grams acetic acid, besides much carbon dioxide which was not accurately determined.

On the Preparation and Properties of Mesoxalic Acid.—By far the best method for preparing mesoxalic acid in quantity is the one recently described by Curtiss[2] from malonic ether and nitrous acid. I obtained with ease, by this method, a

[1] Ber. d. chem. Ges., **17**, 841.
[2] This Journal, **35**, 480.

yield of 65 per cent of the theory of the crystallized acid melting at 115°. It generally contains small amounts of oxalic acid, from which it may be freed by crystallization from ether, or from a mixture of ether and benzene. The pure dihydroxymalonic acid was found to melt at 121°. The presence of oxalic acid can easily be detected and the amount of this impurity present determined quantitatively by titration in alkaline solution with N/10 permanganate (see above).

The following experiment shows that mesoxalic acid, when heated in concentrated aqueous solution to 100°, is slowlv and quantitatively transformed, with evolution of carbon dioxide, into glyoxylic acid—a reaction which is perfectly analogous to the conversion of malonic acid into acetic acid by heat.

Four grams of mesoxalic acid, containing, as determined by titration, 2 per cent of oxalic acid, were heated with 80 cc. water under a reflux condenser for forty hours, in a bath kept at 110°–115°.

On distilling off the water under diminished pressure, 3.04 grams of a pale-yellow, sticky solid, melting from 95° to 105°, remained behind. This substance was quite soluble in water, ether, ethyl acetate and acetone, but insoluble in benzene and in ligroin. It consisted mainly of glyoxylic acid, for, on treatment in aqueous solution with 4.8 grams phenylhydrazine and 5 cc. 50 per cent acetic acid, 5.2 grams of crude, insoluble phenylhydrazones, melting at 136°, were obtained. These were dissolved in sodium carbonate, reprecipitated by acetic acid, and then freed from 0.5 gram insoluble and colorless phenylhydrazine oxalate by crystallization from 70 per cent alcohol. Three and two-tenths grams of the phenylhydrazone of glyoxylic acid were thus obtained in yellow needles melting at 144°.

0.2019 gram substance gave 31.1 cc. N at 22°.5 and 751 mm.

0.1301 gram substance gave 0.2756 gram CO_2 and 0.0617 gram H_2O.

	Calculated for $C_3H_2N_2O_4$.	Found.
C	58.54	57.77
H	4.88	5.27
N	17.07	17.22

In a second experiment, in which 1.31 grams dihydroxymalonic acid and 20 cc. water were heated for forty-nine hours at 100°, the amount of carbon dioxide evolved was determined quantitatively as 0.4 gram (98 per cent of the theory), by absorption in barium hydroxide.

It is well known that alkaline solutions of mesoxalic acid are slowly converted at higher temperatures into oxalic acid. Since mesoxalic acid, as shown by its behavior towards alkaline permanganate, etc., must be dissociated according to

$$CO(COOH)_2 \rightleftharpoons >CO + (COOH)_2,$$

it should be possible to convert this substance, by means of caustic alkalies, quantitatively into molecular quantities of formic and oxalic acid. This is the case, but it was found that prolonged heating of mesoxalic acid, even with concentrated solutions of potassium hydroxide, at 100°, causes very little change. It is necessary to raise the temperature to 150°, when a very rapid transformation in the direction indicated takes place. A mixture of 5 grams of 98 per cent dihydroxymalonic acid, 20 grams of potassium hydroxide, and 20 cc. water was heated in an oil bath kept at 150° for six hours. On working up in the usual manner, by treatment with hydrogen chloride, etc., 4.2 grams crystallized oxalic acid, melting at 100°, or after loss of water of crystallization at 184°, and 0.906 gram formic acid were obtained.

On the Preparation and Reactions of 1,2-Diketobutyric Ether, $CH_3.CO.CO.COOC_2H_5$.—The α,β- or 1,2-diketobutyric ether has recently been prepared by Bouveault[1] from acetoacetic ether, dissolved in acetic anhydride, by means of nitrous acid. The yield is poor because of the simultaneous formation of large amounts of acetylisonitrosoacetoacetic ether.

I have found that the best method for preparing the first-named substance in quantity is to treat crude isonitroso-

[1] Bull. Soc. Chim. [3], **33**, 475–481.

acetoacetic ether, dissolved in ether, with dry nitrous acid, as obtained by the action of concentrated nitric acid on arsenious oxide. Ninety grams of acetoaceticether were mixed with 60 grams of powdered sodium nitrate; a cold solution containing 38 grams of sulphuric acid and 225 cc. water was slowly added to this mixture, which was well cooled by means of ice and salt. After standing for two hours, 200 cc. water and ether, in all 600 cc., were added. After drawing off the ether and drying with calcium chloride, the ethereal solution of isonitrosoacetoacetic ether thus obtained was treated with a rapid stream of nitrous acid at 10°, for three hours. The mixture was now allowed to stand for two days and was then fractionated, finally under diminished pressure. Sixty-nine and three-tenths grams crude diketobutyric ether, boiling from 70°–85° under 18 mm. pressure, were thus obtained. The mobile, yellow oil was freed from acetic and nitric acids by dissolving in an equal weight of water, shaking in the cold with excess of powdered calcium carbonate, extracting 15 times with ether and drying the ethereal extract thus obtained with fused calcium chloride. Forty-six and one-half grams of pure 1,2-diketobutyric ether, boiling from 76°–82° at 18–22 mm. pressure, were thus regularly obtained from 90 grams of acetoacetic ether. This substance has all the properties ascribed to it by Bouveault. It gives a well crystallized hydrate. Phenylhydrazine acetate converts it quantitatively in the cold into the yellow monophenylhydrazone melting at 102°–103°. Aniline acetate, similarly, gives very smoothly the colorless dianilide melting at 117°. I have found that the substance does not reduce Fehling's solution. It should, as a 1,2-dicarbonyl compound, undergo a benzilic acid rearrangement. Such is in fact the case, for even very dilute solutions of sodium carbonate, as well as hydroxide, convert diketobutyric ether very rapidly and quantitatively in the cold into methyltartronic or isomalic acid.

Five grams of the monohydrate of diketobutyric ether, in 10 cc. water, were added to a cold solution of 5.4 grams (4 mols.) sodium hydroxide in 300 cc. water. The solution turned bright yellow at once and, after standing for two days, a slight

excess of hydrogen chloride was added, and the water was then removed by distillation at 18 mm. pressure. On extracting the salt residue with ether, 4.2 grams of practically pure isomalic acid[1] were obtained at once in colorless crystals, melting at 142°

I. 0.2751 gram substance gave 0.3640 gram CO_2 and 0.1158 gram H_2O.

II. 0.2732 gram substance gave 0.3568 gram CO_2 and 0.1127 gram H_2O.

	Calculated for $C_4H_6O_5$.	Found. I.	II.
C	35.82	36.08	35.68
H	4.47	4.67	4.55

A similar experiment with 5 grams diketobutyric ether hydrate, 300 cc. water, and 15 grams (4 mols.) dry sodium carbonate gave, after standing for three days in the cold, acidifying, etc., 3.7 grams of a sticky solid melting at 96°. This consisted of a mixture of methyltartronic acid and the ester acid, for, on digestion with water and an excess of powdered calcium carbonate, no trace of calcium oxalate could be detected. The aqueous filtrate, after concentration and cooling, gave 4.07 grams calcium methyltartronate in the form of white, opaque, not well defined, crystals, difficultly soluble in cold water.

1.056 grams air-dry salt lost 0.0948 gram H_2O when dried over sulphuric acid *in vacuo*, and 0.098 gram more H_2O when dried at 100°–110°.

0.6570 gram anhydrous salt gave, on ignition, 0.2056 gram CaO.

	Calculated for $C_4O_5H_4Ca.2H_2O$.	Found.
H_2O	17.22	16.36
Ca	23.02	22.37

I have found that concentrated aqueous solutions of methyltartronic acid may be heated for days, at 65°, without decomposition; if, however, the solutions are heated in a bath kept at 100° a rapid and quantitative transformation of isomalic acid into carbon dioxide and racemic-lactic acid takes

[1] Schmöger: J. prakt. Chem. [2], **14**, 18; **19**, 168; **24**, 38.

place—a change which has hitherto only been noticed with the solid substance at temperatures above 140°.

Thus, 2 grams isomalic acid and 3 cc. water, heated under a reflux condenser for twenty-seven hours, at 100°, gave 0.58 gram carbon dioxide, from 2.6 grams barium carbonate, and 1.9 grams crystallized zinc lactate.

Diketobutyric Ether and Water.—A solution of 10 grams diketobutyric ether in 10 cc. water loses carbon dioxide very slowly when heated in a bath kept between 63° and 65°. The amount of carbon dioxide given off during seventy-four hours' heating was determined quantitatively as 2.4 grams, from 10.95 grams barium carbonate. The aqueous solution was now made up to 25 cc. and the presence of pyruvic aldehyde, lactic and oxalic acids was established as follows: Three-fifths of the solution, treated in the cold with 10 grams phenylhydrazine dissolved in 10 cc. 50 per cent acetic acid, gave 2.5 grams of a yellow precipitate. This, when digested with benzene, gave 0.42 gram insoluble phenylhydrazine oxalate, crystallizing in colorless plates from 30 per cent alcohol. The benzene filtrate gave, on concentration, 0.9 gram of methylglyoxaldiphenylhydrazone melting at 144°. The remaining 10 cc. of the aqueous solution gave, when digested with powdered basic zinc carbonate, 2.4 grams of zinc lactate crystals. Methyltartronic acid was not found to be present and, since experiments with this acid mentioned above show that it remains unchanged when heated for days in aqueous solution at 65°, it is certain that the large amount of racemic-lactic acid obtained in the experiment under consideration owes its origin to a benzilic acid rearrangement of the pyruvic aldehyde, which is formed from diketobutyric ether by hydrolysis and subsequent loss of carbon dioxide,

$$CH_3.CO.CO.COOC_2H_5 + H_2O \rightarrow CH_3.CO.CO.COOH + C_2H_5OH \rightarrow CH_3COCHO + CO_2 + C_2H_5OH + H_2O.$$

The following analytical results were obtained with the various products isolated in the experiment:

1.1758 grams air-dry zinc lactate, dried seven hours at 100°, lost 0.2137 gram H_2O.

0.5681 gram anhydrous salt gave, on ignition, 0.1907 gram ZnO.

	Calculated for $Zn(C_3H_5O_2)_2.3H_2O$.	Found.
H_2O	18.16	18.18
Zn	26.89	26.92

0.1763 gram diphenylhydrazone gave 0.4624 gram CO_2 and 0.1064 gram H_2O.

0.1545 gram diphenylhydrazone gave 29.8 cc. N at 20° and 751 mm. pressure.

	Calculated for $C_{15}H_{16}N_4$.	Found.
C	71.43	71.54
H	6.35	6.34
N	22.22	21.82

A large amount, over 2 grams, of lactic acid was also obtained from 9.6 grams diketobutyric ether by heating for three and a half hours with 30 cc. 10 per cent sulphuric acid in a bath kept at 130°, and subsequently extracting 10 times with ether, etc.

In an experiment in which 5 grams diketobutyric ether and 22 cc. absolute alcohol were heated in a sealed tube at 100°, for thirty-two hours, the substance was recovered entirely unchanged.

Diketobutyric Ether, Silver Oxide, Etc.—It was now of interest to determine whether silver or mercuric oxide interferes with the conversion of diketobutyric ether by caustic alkalies into methyltartronic acid by a benzilic acid rearrangement. Thus, Evans has found[1] that benzoylformaldehyde, which gives racemic-mandelic acid quantitatively with dilute sodium hydroxide, gives no trace of this acid when silver or mercuric oxide is also present. The preliminary experiments with the analogous, but polymerized, crude acetylformaldehyde, and the quantitative experiment with pure acetol, oxide of mercury and sodium hydroxide, which are described above, prove that in this case there is practically no interference with the transformation of methylglyoxal into racemic-lactic acid when either oxide of mercury or silver is also present. This striking difference in the result can only be

[1] THIS JOURNAL, 35, 118.

explained by the aid of the assumption that in the latter case the speed of the benzilic acid rearrangement is far greater—a conclusion which is also justified by the fact that pyruvic aldehyde gives lactic acid in aqueous solution at 65°, whereas benzoylformaldehyde remains entirely unchanged under similar treatment.

Corresponding experiments with 1,2-diketobutyric ether and caustic alkalies in the presence of oxide of silver or mercury now show that here, too, there is practically no interference with the conversion into isomalic acid. In this case, however, another reaction is also observed to take place simultaneously and is, in fact, the predominant one, especially if silver oxide without alkali be used.

When diketobutyric ether is treated in the cold with water and well washed silver oxide, molecular amounts of acetic and oxalic acids are obtained. This reaction can only be explained by the assumption that dissociated molecules of 1,2-diketobutyric ether hydrate,

$$CH_3C(OH)_2—CO—COOC_2H_5 \rightleftharpoons CH_3COOH + HCO.COOC_2H_5,$$

or

$$CH_3—CO—C(OH)_2COOC_2H_5 \rightleftharpoons CH_3CHO + COOH.COOC_2H_5,$$

are also present in addition to those produced according to

$$CH_3CO.CO.COOC_2H_5 \rightleftharpoons CH_3.CO.COOC_2H_5 + >C=O,$$

which account for the benzilic acid rearrangement.

Now, it has long been known that dibenzil, which also undergoes the benzilic acid rearrangement with caustic alkalies, is split by aqueous solutions of sodium carbonate or potassium cyanide[1] into molecular quantities of benzoic aldehyde and benzoic acid—a reaction which is perfectly analogous to the one under consideration.

Five grams of diketobutyric ether in 50 cc. water were slowly added to 3.5 molecules of freshly precipitated and well washed silver oxide, suspended in about 200 cc. water. Re-

[1] Michael and Palmer: THIS JOURNAL, 7, 191. Jourdan: Ber. d. chem. Ges., 18, 658.

duction to silver took place at once in the cold, and after two days' standing, during which time no evolution of carbon dioxide was noticed, the silver salts present were decomposed by hydrogen sulphide. The amount of silver present was then determined as 7.2 grams by dissolving the insoluble sulphide in 40 per cent cyanide of potash solution. The aqueous filtrate, freed from hydrogen sulphide, was worked up as usual by distillation at reduced pressure. The oxalic acid was, therefore, left in the non-volatile portion, whereas the aqueous distillate which did not reduce alkaline permanganate, and was made up to a volume of half a liter, contained acetic acid only. Fifty cc. of this distillate required 34.7 cc. N/10 potassium hydroxide for neutralization, hence 2.08 grams of acetic acid were present. Three and four-tenths grams of crystallized oxalic acid, melting at 98°, were obtained from the non-volatile residue by means of ether. This, when digested with water and powdered calcium carbonate and subsequently with 10 per cent acetic acid, gave 4 grams insoluble calcium oxalate.

A second experiment was carried out in which 5 grams of diketobutyric ether, in 50 cc. water, were slowly added, with thorough cooling, to a mixture containing about 200 grams water, 7 grams (5 mols.) sodium hydroxide, and 1.25 molecules silver oxide (from 14.3 grams silver nitrate). Reduction to silver took place with marked evolution of heat. After standing for two days and working up quantitatively, as usual, 0.22 gram carbon dioxide (from 0.95 gram barium carbonate) and 4.03 grams of non-volatile crystalline acids were obtained. The latter product was resolved by digestion with powdered calcium carbonate, etc. into 3.24 grams calcium isomalate and 1.9 grams calcium oxalate. The amount of potassium hydroxide required for neutralizing the total aqueous distillate (volume, 500 cc.) was determined as 0.857 gram, and 50 cc. of the distillate required 19.9 cc. N/10 permanganate for oxidation. This shows that small amounts of formic as well as of acetic acid must be present.

A special experiment with methyl tartronic acid, dilute sodium hydroxide and freshly precipitated oxide of silver

proved that on standing for twenty-four hours, at ordinary temperatures, no trace of metallic silver is formed, the isomalic acid being furthermore recovered entirely unchanged. Diketobutyric ether, in aqueous alcoholic solution, has not the slightest action on freshly precipitated and well washed oxide of mercury, even on standing for days in the cold. When, however, 5 grams of diketobutyric ether in 50 cc. water were added to a mixture containing 1.25 molecules of oxide of mercury, 150 cc. water and 3.4 grams (2.5 mols.) sodium hydroxide, a slight reduction to mercury was noticed at once in the cold. After standing for two days, filtering, etc., 4.3 grams of crystalline acids were obtained by extracting the salt residue with ether. These gave, on digestion with powdered calcium carbonate, etc., 2.4 grams of calcium isomalate and 2.3 grams of calcium oxalate. A portion of the calcium methyltartronate obtained was converted by means of oxalic acid into free isomalic acid, melting at 140°.

In conclusion, the writer wishes to acknowledge her sense of appreciation for the continual help and encouragement given by Dr. Nef throughout the course of this work.

Contributions from the Sheffield Laboratory of Yale University.

CXLIX. — RESEARCHES ON PYRIMIDINES: SYNTHESIS OF CYTOSINE-5-CARBOXYLIC ACID.

(TWENTY-SIXTH PAPER.)

BY HENRY L. WHEELER AND CARL O. JOHNS.

The present work was undertaken with the object of making a study of some material to be used for further syntheses, and also in order to examine the properties of cytosine-5-carboxylic acid and some of its derivatives. The acid has now been prepared by means of the following reactions: In a previous paper[1] we showed that ethoxymethylenmalonic ester,

$$C_2H_5OCH=C(CO_2C_2H_5)_2,$$

in alkaline solution, condenses normally with ethylpseudothiourea, $H_2N—C(SC_2H_5)=NH$, giving 2-ethylmercapto-5-

[1] THIS JOURNAL, 27, 392 (1907).

carbethoxy-6-oxypyrimidine (I.). We now find that this cyclo amide reacts smoothly with phosphorus oxychloride, yielding an oil which is the imide chloride, 2-ethylmercapto-5-carbethoxy-6-chlorpyrimidine (II.). The transformation of this into 2-ethylmercapto-5-carbethoxy-6-aminopyrimidine (III.), on standing with alcoholic ammonia at ordinary temperature, is also a perfectly smooth reaction. The imide chloride, therefore, in this case, is far more reactive than 2-ethylmercapto-6-chlorpyrimidine. The latter does not react on standing overnight with alcoholic ammonia, but it does react in a short time at 120°.

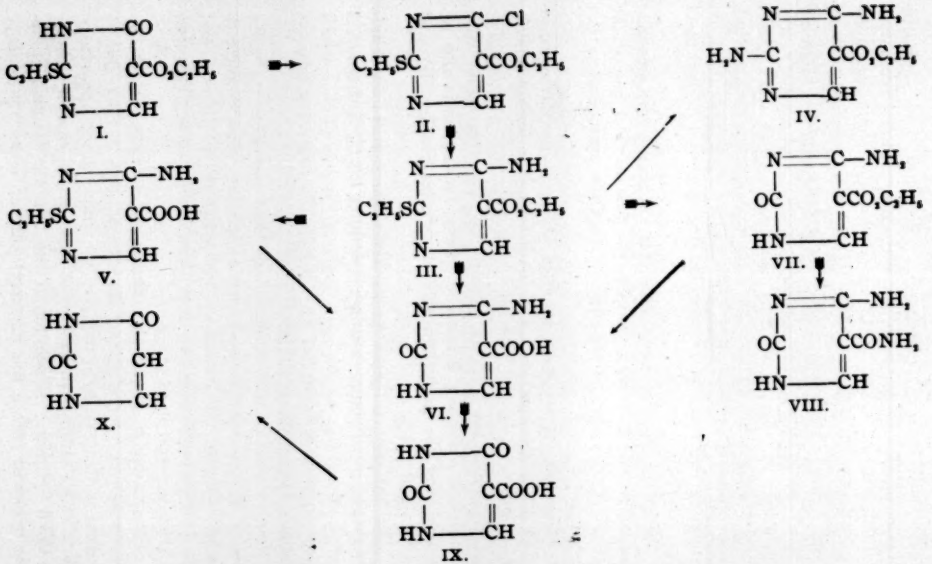
When the mercaptoamino ester (III.) is heated with alcoholic ammonia the mercapto group is the first to be removed (at about 170°) and 2,6-diamino-5-carbethoxypyrimidine (IV.) results.

When the mercaptoamino ester (III.) is carefully warmed with dilute alcoholic potassium hydroxide it is readily saponified and a potassium salt of 2-ethylmercapto-5-carboxyl-6-amino-pyrimidine (V.) is formed. If the treatment with potassium hydroxide is more energetic, mercaptan is also removed and the potassium salt of cytosine-5-carboxylic acid is obtained (VI.).

The moderate action of strong hydrochloric acid on 2-ethylmercapto-5-carbethoxy-6-aminopyrimidine (III.) first removes ethylmercaptan, giving 5-carbethoxycytosine (VII.), which with aqueous ammonia at 150° is partially converted into cytosine-5-carboxamide (VIII.).

Longer boiling with hydrochloric acid saponifies the ester (III.), both mercaptan and alcohol separate, and cytosine-5-carboxylic acid (VI.) results. The synthesis of the acid and the transformations of the new pyrimidines can be illustrated by the formulas on page 596.

The action of acids on cytosine-5-carboxylic acid (VI.) developed the interesting fact that the presence of the carboxyl radical in the 5-position rendered the amino group apparently more easily subject to hydrolysis than in the case of unsubstituted cytosine. It was found also that the 6-amino group was removed before the carboxyl radical when cytosine-5-

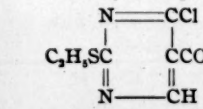

I.
II.
III.
IV.
V.
VI.
VII.
VIII.
IX.
X.

carboxylic acid was boiled with 20 per cent sulphuric acid, the chief product obtained being uracil-5-carboxylic acid (IX.), while only a small amount of cytosine was formed. Unless groups attached to cytosin-5-carboxylic acid would alter the course of hydrolysis, these results exclude the possibility that cytosin exists in the nucleic acids in the form of a 5-carboxyl derivative, or, in other words, it is not a grouping of this sort which is the source of cytosine.

Further action of acids, either at a high temperature, or on more prolonged boiling, strips all of the groups from the above compounds, leaving uracil (X.) as the last pyrimidine to be obtained.

EXPERIMENTAL PART.

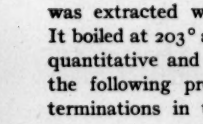
2-Ethylmercapto-5-carbethoxy-6-chlorpyrimidine,



—Thirteen grams of 2-ethyl-mercapto-5-carbethoxy-6-oxypyrimidine were boiled for two and a half hours with 40 cc. of phosphorus oxychloride. The phosphorus oxychloride was then removed by evaporation at 100° under diminished pressure. This left a syrup which was treated with cracked ice and the resulting oil, which did not solidify, was extracted with ether and dried over calcium chloride. It boiled at 203° at 20 mm. pressure. The yield of oil is almost quantitative and the crude product is pure enough to use for the following preparations without distilling. Nitrogen determinations in the case of the distilled product gave:

	Calculated for $C_9H_{11}O_4N_2SCl$.	Found. I.	II.
N	11.35	11.33	11.31

2-Ethylmercapto-5-carbethoxy-6-aminopyrimidine,



—Fourteen grams of 2-ethylmercapto-5-carbethoxy-6-chlorpyrimidine were added to a cold saturated

solution of alcoholic ammonia in a bottle. A reaction set in almost at once and a mass of crystals separated. The bottle was kept cool by means of ice-water. The material was allowed to stand overnight and then the alcohol and ammonia were evaporated and the residue treated with water. The yield was 90 per cent of the calculated. The resulting product melted to an oil in hot water but did not dissolve. It dissolved readily in hydrochloric acid. It was easily soluble in hot and moderately soluble in cold alcohol from which solvent it crystallized in rectangular plates melting at 102°. Analysis:

	Calculated for $C_9H_{13}O_3N_3S$.	Found. I.	II.
N	18.50	18.41	18.42

When this substance was boiled with strong hydrochloric acid for about one hour, the solution evaporated to dryness and the residue dissolved in sodium hydroxide and precipitated with acetic acid, cytosine-5-carboxylic acid was obtained.

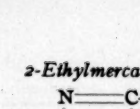
2,6-Diamino-5-carbethoxypyrimidine, $H_2N-C(=N-CH)-C(=CCO_2C_2H_5)-C(=N)-NH_2$.

—This was obtained by heating the above 2-ethylmercapto-5-carbethoxy-6-aminopyrimidine with a saturated solution of alcoholic ammonia at 168°-178° for one and a half hours. When the tube became cool, a solid separated. The material was difficultly soluble in cold alcohol and water and it crystallized from alcohol in the form of needles melting to a clear oil at 205°–207°. Analysis:

	Calculated for $C_7H_{10}O_2N_4$.	Found. I.	II.
N	30.76	30.62	30.76

This substance is soluble in hydrochloric acid from which solution it is reprecipitated by ammonia. The material which remained in the alcoholic mother-liquor from the above was found to be unaltered mercapto-derivative. Under the conditions of the experiment it appears that the carbethoxy group was not attacked.

2-Ethylmercapto-5-carboxyl-6-aminopyrimidine,

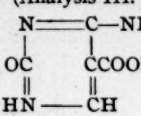


.—When 2-ethylmercapto-5-carbethoxy-6-aminopyrimidine in alcoholic solution was treated with an equal weight of potassium hydroxide in a small amount of water it was readily saponified. On evaporating to dryness the resulting residue dissolved easily in water. When this solution was made acid with acetic acid a white crystalline substance slowly separated. This was slightly soluble in hot water and difficultly soluble in hot alcohol, from which it crystallized in microscopic prisms. It decomposed with effervescence at 230°. It was very soluble in ammonia and also in an excess of hydrochloric acid. Analysis:

	Calculated for $C_7H_9O_2N_3S$.	Found. I.	II.
N	21.10	20 95	21.04

During the above hydrolysis there was a decided odor of escaping mercaptan. In order to determine whether mercaptan could be conveniently split off by means of potassium hydroxide, another portion of 2-ethylmercapto-5-carbethoxy-6-aminopyrimidine was heated a little longer on the steam-bath with somewhat more than 2 molecular proportions of potassium hydroxide. On acidifying the residue, a substance was obtained which did not contain sulphur and agreed in properties with cytosine-5-carboxylic acid. (Analysis III. below.)

Cytosine-5-carboxylic Acid,



.—This amino acid was first prepared by evaporating the above mercaptoamino acid with concentrated hydrochloric acid on the steam-bath. After evaporating once with a moderate amount of acid, the residue was taken up in water and evaporated again to remove hydrochloric acid. It was found that the acid was almost insoluble in hot water, alcohol and acetic acid. The specimen

used for analysis was purified by dissolving in ammonia and precipitating with acetic acid. It came down in a very finely divided state and was hard to filter. It decomposed with effervescence at 256°-257°. Analysis:

	Calculated for $C_5H_5O_2N_3$.	Found. I.	II.	III.
N	27.09	27.07	27.07	26.80

To prepare this acid it is not necessary to isolate the 2-ethylmercapto-5-carboxyl-6-aminopyrimidine. The easiest way is to start with 2-ethylmercapto-5-carbethoxy-6-aminopyrimidine and evaporate this once with an equal weight of potassium hydroxide in dilute alcohol. Concentrated hydrochloric acid is then added to the residue and the evaporation carried on again to dryness. The mixture is taken up in water, to remove potassium chloride, and, on filtering and washing with water, the acid is obtained in an almost pure condition. The aqueous solution of cytosine-5-carboxylic acid does not give a precipitate with barium chloride, picric acid or lead acetate. It gives but a slight turbidity with silver nitrate.

Action of Twenty Per Cent Sulphuric Acid: Formation of Uracil-5-carboxylic Acid. — One gram of cytosine-5-carboxylic acid was boiled on a return condenser for 20 hours with 40 cc. of sulphuric acid. A solid separated on cooling. It weighed 0.5 gram. This was crystallized from water and came down in clusters of pointed, microscopic prisms which decomposed at 277°. They were indentified as uracil-5-carboxylic acid. Analysis: 0.3133 gram substance lost 0.0329 gram water at 120°–130°.

	Calculated for $C_5H_4O_4N_2.H_2O$.	Found.
H_2O	10.34	10.50
N	17.94	18.22

A duplicate experiment performed as above gave 0.45 gram of uracil-5-carboxylic acid, which separated from the solution. After filtering from this, the sulphuric acid was removed and the solution concentrated to 10 cc., then precipitated with picric acid. This gave 0.17 gram picrate, crystallizing in needles, equal to 0.06 gram cytosin.

Formation of Uracil.—One half gram of cytosine-5-carbox-

ylic acid was heated with 5 cc. of 20 per cent sulphuric acid at 162°–167° for 2 hours. On opening the sealed tube, considerable pressure was noticed and a deposit which had the appearance of uracil had separated. This was recrystallized from water and identified as uracil. Analysis:

	Calculated for $C_4H_4O_2N_2$.	Found.
N	25.00	24.97

Action of Concentrated Hydrochloric Acid: Formation of Uracil.—One gram of cytosine-5-carboxylic acid was boiled with 50 cc. of concentrated hydrochloric acid, using a return condenser, for 22 hours. The acid was then evaporated and the residue was treated with boiling water. A small portion was insoluble in hot water. This was unaltered cytosine-5-carboxylic acid; an analysis gave 26.80 per cent of nitrogen while the calculated is 27.09 per cent.

The portion which was soluble in water crystallized in balls like uracil. Analysis gave 24.90 per cent nitrogen.

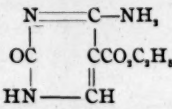
Cytosine-5-carboxylic Acid Hydrochloride was prepared by crystallizing some of the acid from 20 per cent hydrochloric acid. It formed ragged pointed prisms which melted at 275°–276° and it contained a molecule of water of crystallization.

Analysis:

0.1327 gram lost 0.0117 gram of water at 130°–140°.

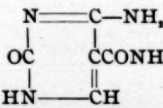
	Calculated for $C_5H_5O_2N_3.HCl.H_2O$.	Found.
H_2O	8.59	8.82

	Calculated for $C_5H_5O_2N_3.HCl$.	Found.
N	21.93	21.71

5-Carbethoxycytosine,  , was formed by evaporating 2-ethylmercapto-5-carbethoxy-6-aminopyrimidine with concentrated hydrochloric acid on the steam bath. The product was dissolved in hot water and the solution after making slightly alkaline with ammonia gave needles which

browned and decomposed slowly at about 260°–275°. This ester was only slightly soluble in hot alcohol. Analysis:

	Calculated for $C_7H_9O_2N_3$.	Found. I.	II.
N	22.95	22.97	23.00



Cytosine-5-carboxamide, OC CCONH$_2$.—The action of HN—CH

concentrated aqueous ammonia on the above ester was not at all smooth. In one experiment in which the ester was heated with concentrated ammonia for 2 hours at 140°–150°, about 25 per cent of the material remained unaltered but on evaporating the mother-liquor far more soluble material was obtained. This crystallized in tufts of hair-like needles. It was recrystallized from water. (Analysis I.) On heating, no definite melting or decomposition point was observed.

Analyses of two different samples gave the following results which show that the expected amide had been obtained.

	Calculated for $C_5H_5O_2N_3$.	Found. I.	II.
N	36.36	35.94	35.00

NEW HAVEN, CONN.,
May, 1907.

CL.—RESEARCHES ON PYRIMIDINES: SYNTHESIS OF THYMINE-5'-CARBOXYLIC ACID.

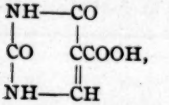
[TWENTY-SEVENTH PAPER.]

BY TREAT B. JOHNSON AND CARL FRANK SPEH.

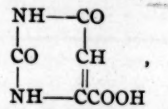
The possibilty that uraeil, cytosine and thymine might be linked in nucleic acids by acid amide or polypeptide groupings was an incentive to make a thorough study of the carboxyl derivatives of these pyrimidines. Descriptions of uracil-5-carboxylic acid,[1] I., thymine-4-carboxylic acid,[2] IV., cytosine-5-carboxylic acid,[3] III., and uracil-4-carboxylic acid,[4]

[1] Wheeler, Johnson and Johns: THIS JOURNAL, **27**, 392.
[2] Johnson: Jour. Biolog. Chem., **2**, 299.
[3] Wheeler and Johns: THIS JOURNAL, **28**, 594.
[4] Wheeler: *Ibid.*, **28**, 358.

II., have already been published in papers from this laboratory.



I.



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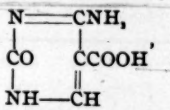
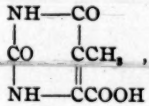
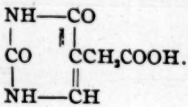


III.

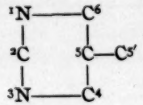


IV.

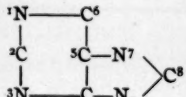


V.

We shall describe in this paper the preparation and properties of thymine-5′-carboxylic acid, V. The carbon atom in the methyl radical of thymine is designated 5′ in order to avoid confusion and to distinguish from position 7 in the purine molecule. We find that this acid, V.,



Pyrimidine.



Purine.

can be heated with 20 per cent sulphuric acid at 160°–170° without alteration. *Thymine, therefore, cannot exist in nucleic acids as a 5′-carboxyl compound.*

The information acquired by investigating these pyrimidine acids has advanced decidedly our knowledge of the structure of the nucleic acid molecule. The results of our work justify us in concluding that uracil is the only one of the three pyrimidines—uracil, cytosine and thymine—that can be linked in nucleic acids by an acid amide grouping—CO.NH. *Uracil might exist as a 5-carboxyl compound.* This conclusion is supported by the fact that uracil-5-carboxylic acid,[1] I., is quantitatively converted into uracil when heated with 20 per cent sulphuric acid at 160°–170°. Uracil-4-carboxylic acid,[1] II., and thymine-4-carboxylic acid,[1] IV., could be heated under

[1] *Loc. cit.*

the same conditions without alteration. The possibility of cytosine being linked as a 5-carboxyl compound is excluded, since cytosine-5-carboxylic acid,[1] III., is changed to uracil-5-carboxylic acid by hydrolysis with dilute sulphuric acid.

Every α-derivative of ethyl β-oxyacrylate (ethylformylacetate) that we have examined in this laboratory has condensed with a pseudothiourea, in presence of alkali, giving a 2-mercapto pyrimidine, *viz.*:

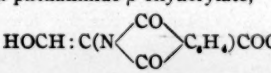
1. Ethyl β-oxyacrylate,[2]

$$HOCH:CH.COOC_2H_5.$$

2. Ethyl α-methyl-β-oxyacrylate,[3]

$$HOCH:C(CH_3)COOC_2H_5.$$

3. Ethyl α-phthalimido-β-oxyacrylate,[4]



4. Ethyl α-benzoylamino-β-oxyacrylate,[5]

$$HOCH:C(NHCOC_6H_5)COOC_2H_5.$$

5. Ethyl α-phenyl-β-oxyacrylate,[6]

$$HOCH:C(C_6H_5)COOC_2H_5.$$

6. Ethyl α-urethane-β-oxyacrylate,[7]

$$HOCH:C(NHCOOC_2H_5)COOC_2H_5.$$

7. Ethyl α-ethoxy-β-oxyacrylate,[8]

$$HOCH:C(OC_2H_5)COOC_2H_5.$$

8. Ethyl α-ethyl-β-oxyacrylate,[9]

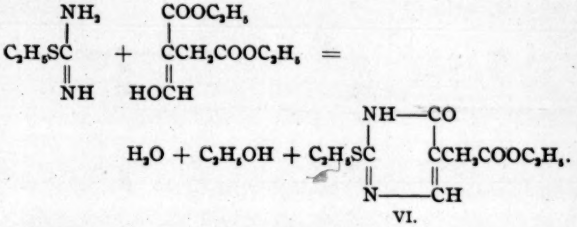
$$HOCH:C(C_2H_5)COOC_2H_5.$$

9. Ethyl α-phenoxy-β-oxyacrylate,[10]

$$HOCH:C(OC_6H_5)COOC_2H_5.$$

[1] *Loc. cit.*
[2] Wheeler and Merriam: THIS JOURNAL, **29**, 478.
[3] Wheeler and Merriam: *Loc. cit.*
[4] Johnson and Clapp: THIS JOURNAL, **32**, 130.
[5] Johnson and Clapp: *Loc. cit.*
[6] Wheeler and Bristol: THIS JOURNAL, **33**, 448.
[7] Johnson: *Ibid.*, **34**, 191.
[8] Johnson and McCollum: Jour. Biolog. Chem., **1**, 437. THIS JOURNAL, **36**, 149.
[9] Johnson and Menge: Jour. Biolog. Chem., **2**, 105.
[10] Johnson and Heyl: THIS JOURNAL, **37**, 628.

We now find that the sodium salt of diethyl formylsuccinate condenses in a smooth manner with pseudoethylthiourea, giving ethyl 2-ethylmercapto-6-oxypyrimidine-5-acetate, VI. The condensation is represented by the following equation:



VI.

When ethyl 2-ethylmercapto-6-oxypyrimidine-5-acetate, VI., was digested with concentrated hydrochloric acid, or with alcohol and hydrochloric acid, it was converted quantitatively into thymine-5′-carboxylic acid, VIII. Esterification of thymine-5′-carboxylic acid with ethyl alcohol and sulphuric acid gave thymine-5′-ethylcarboxylate, IX. 2-Ethylmercapto-6-oxypyrimidine-5-acetic acid, VII., was obtained when ethyl 2-ethylmercapto-6-oxypyrimidine-5-acetate, VI., was saponified with an alcoholic solution of potassium hydroxide. When this mercapto acid was digested with hydrochloric acid it was converted into thymine-5′-carboxylic acid.

Ethyl 2-ethylmercapto-6-oxypyrimidine-5-acetate, VI., reacts in a smooth manner with phosphorus oxychloride, giving 2-ethylmercapto-6-chlorpyrimidine-5-acetic acid, X. When the mercapto ester, VI., was heated with ammonia it was converted into 2-ethylmercapto-6-oxypyrimidine-5-acetamide, XI., and 2-amino-6-oxypyrimidine-5-acetamide, XII. These different transformations are represented by the formulas on the following page.

Thymine-5′-carboxylic acid is difficultly soluble in water and melts at about the same temperature as thymine (315°–320°). It crystallizes from water in anhydrous condition. It is a strong acid and gives an insoluble, crystalline lead salt,

NH—CO
CO
NH
CCH2COOC2H5
CH
IX.
NH—CO
CO
NH
CCH2COOH
CH
VIII.
NH—CO
C2H5SC
N
CCH2COOC2H5
CH
VI.
NH—CO
H2NC
N
CCH2CONH2
CH
XII.
NH—CO
C2H5SC
N
CCH2COOH
CH
VII.
NH—CO
C2H5SC
N
CCH2CONH2
CH
XI.
N—CCl
C2H5SC
N
CCH2COOH
CH
X.

Vol.
19

when lead acetate is added to its aqueous solution. It was not precipitated by phosphotungstic acid. Addition of barium chloride to aqueous solutions of the acid produced no precipitate. Potassio-bismuth iodide gave a yellow, crystalline precipitate.

EXPERIMENTAL PART.

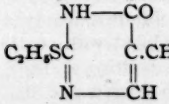
Diethyl Formylsuccinate, $CHO.CH.COOC_2H_5$ / $CH_2.COOC_2H_5$.—The sodium salt of this ester was prepared by condensing ethyl formate with diethyl succinate in presence of metallic sodium. Eleven grams of sodium wire were suspended in anhydrous ether and a mixture of molecular proportions of ethyl formate and diethyl succinate slowly added. There was an immediate reaction with evolution of hydrogen gas and the ether assumed a red color. The mixture was allowed to stand for ten to twelve hours and then shaken with cold water to dissolve the sodium salt of diethyl formylsuccinate. When this aqueous solution was acidified with hydrochloric acid the free ester separated as a heavy yellow oil. After drying, in ether solution with calcium chloride it was distilled under diminished pressure. The fraction that was analyzed boiled at 158°–160° under 20 mm. pressure.

I. 0.4614 gram substance gave 0.8994 gram CO_2 and 0.2816 gram H_2O.

II. 0.5762 gram substance gave 1.1107 grams CO_2 and 0.3573 gram H_2O.

	Calculated for $C_9H_{14}O_5$.	Found. I.	II.
C	53.4	53.16	52.58
H	6.93	6.79	6.89

Ethyl 2-Ethylmercapto-6-oxypyrimidine-5-acetate,



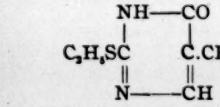
C_2H_5SC ‖ $C.CH_2COOC_2H_5$.—One hundred and sixty-five grams of diethyl succinate and one molecular proportion of ethyl formate were condensed in presence of the required

amount of metallic sodium, as described in the previous experiment. The sodium salt of diethyl formylsuccinate was then dissolved in cold water and added to an aqueous solution of 109 grams of pseudoethylthiourea hydrobromide. A molecular proportion of potassium hydroxide was then added and the mixture allowed to stand for seven to eight hours at ordinary temperature. It was then heated on the steam-bath for three hours and cooled, when prismatic crystals of the mercapto pyrimidine deposited. When the alkaline solution was acidified with acetic acid, more of the pyrimidine separated. The compound was practically insoluble in cold water, but dissolved in boiling water and separated, on cooling, in well developed, prismatic crystals. It crystallized from alcohol in slender needles melting at 146°–147°, with no effervescence. It crystallized from water without water of crystallization. The yield of crude pyrimidine was 80 grams. Analysis (Kjeldahl):

	Calculated for $C_{10}H_{14}O_2N_2S$.	Found. I.	II.
N	11.57	11.60	11.55

In two other experiments we obtained 22 grams and 38 grams of the mercapto pyrimidine from 63 grams and 90 grams of diethyl succinate, respectively.

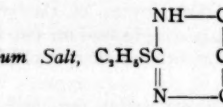
2-Ethylmercapto-6-oxypyrimidine-5-acetic Acid,



C_2H_5SC $C.CH_2COOH$.—This acid was prepared by saponifying the ethyl ester with potassium hydroxide. Ten grams of the ester and 3 grams of potassium hydroxide were digested in alcohol for about twelve hours. The alkaline solution was then evaporated to dryness and the residue obtained dissolved in warm water. This solution was then acidified with acetic acid, when about 1 gram of unaltered ester, melting at 146°, separated. After evaporating the filtrate to dryness and dissolving the residue again in a little water, the solution was acidified with a few drops of dilute hydrochloric acid. The

mercapto acid separated at once and crystallized from hot water in needles and square plates melting at 184°, with evolution of carbon dioxide and ethylmercaptan. When digested with hydrochloric acid it was converted into *thymine-5'-carboxylic acid* (see below). Analysis (Kjeldahl):

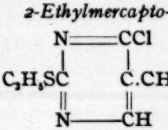
	Calculated for $C_8H_{10}O_3N_2S$.	Found. I.	II.
N	13.08	12.9	12.85



The Potassium Salt, $C_2H_3SC(=N-CH)-CCH_2COOK$.—This salt was extremely soluble in water and alcohol. It separated from very concentrated, aqueous solutions in long needles. They did not contain water of crystallization. Analysis (Kjeldahl):

	Calculated for $C_8H_9O_3N_2SK$.	Found.
N	11.11	11.31

2-Ethylmercapto-6-chlorpyrimidine-5-acetic Acid



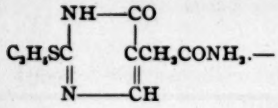
$C_2H_3SC(=N-CH)-C.CH_2COOH$.—Ethyl 2-ethylmercapto-6-oxypyrimidine-5-acetate dissolves at once in cold phosphorus oxychloride, with no evolution of heat. Fifteen grams of the pyrimidine were dissolved in 50 cc. of phosphorus oxychloride and the solution boiled gently for two and a half hours. It was then allowed to stand for five to six hours and poured upon crushed ice to destroy the excess of phosphorus halides. We obtained a dark colored solution, which was extracted several times with ether. This ether solution was then thoroughly washed with sodium hydroxide solution and the alkaline washings saved. When they were neutralized with hydrochloric acid the chlorpyrimidine separated in granular crystals. The yield was 8.5 grams. The pyrimidine was difficultly soluble

in water and very soluble in alcohol. It crystallized from alcohol in clusters of prismatic crystals, melting at 132°, to a clear oil. When heated above its melting point it decomposed with violent effervescence. Analysis (Kjeldahl):

	Calculated for $C_9H_9O_3N_2SCl$.	Found. I.	II.
N	12.07	11.9	12.02

Action of Alcoholic Ammonia on Ethyl 2-Ethylmercapto-6-oxypyrimidine-5-acetate.—Two grams of the pyrimidine and 25 cc. of alcoholic ammonia were heated for two hours at 140°–150°. When the tube was opened there was no pressure but there was a strong odor of ethyl mercaptan. We obtained a deposit of crystalline material, which was very soluble in hot water and separated, on cooling, in prismatic crystals associated with some needles. By a fractional crystallization from water we finally separated a compound which melted at 214°, with slight effervescence. It responded to a test for sulphur and a nitrogen determination agreed with the calculated value in

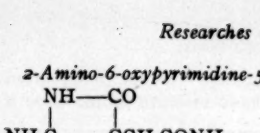
2-Ethylmercapto-6-oxypyrimidine-5-acetamide,



	Calculated for $C_8H_{11}O_3N_3S$.	Found.
N	19.75	19.58

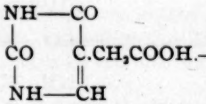
In a second experiment, 4 grams of the mercapto ester and 50 cc. of alcoholic ammonia were heated for two hours at 170°–180°. When the tube was examined there was no pressure but a strong odor of mercaptan, and small, granular crystals were suspended in the alcohol. These were removed and recrystallized from water. On cooling, prismatic crystals separated, which charred at 260°–266° and then decomposed at about 280°, with violent effervescence. They did not respond to a test for sulphur and a nitrogen determination agreed with the calculated value in

2-Amino-6-oxypyrimidine-5-acetamide,



	Calculated for $C_6H_8O_2N_4$.	Found. I.	II.
N	33.33	32.6	32.75

Thymine-5'-carboxylic Acid,



—This acid was obtained when ethyl 2-ethylmercapto-6-oxypyrimidine-5-acetate was digested in alcoholic solution with hydrochloric acid. Five grams of the mercapto ester were dissolved in a mixture of 20 cc. of alcohol and 5 cc. of concentrated hydrochloric acid and the solution heated on the steam-bath for 2.5 hours. The pyrimidine separated as a colorless, crystalline powder that was practically insoluble in alcohol. A quantitative yield of the acid was also obtained when ethyl 2-ethylmercapto-6-oxypyrimidine-5-acetate or 2-ethylmercapto-6-oxypyrimidine-5-acetic acid was digested with concentrated hydrochloric acid (Analyses IV. and V.). Analysis (Kjeldahl):

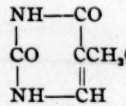
	Calculated for $C_6H_6O_4N_2$.	Found. I.	II.	III.	IV.	V.
N	16.47	16.28	16.12	16.28	16.5	16.5

Thymine-5'-carboxylic acid was very insoluble in cold water but crystallized from boiling water in microscopic, granular crystals, which generally melted at 315°–320°, with decomposition. It did not contain water of crystallization, and when mixed with thymine the melting-point was lowered to 290°–300°. Its aqueous solution gave a strong acid reaction when tested with blue litmus. It was precipitated by silver nitrate and mercuric chloride in weak ammoniacal solutions. The silver salt dissolved in excess of ammonia. Copper carbonate was decomposed by the acid, giving an insoluble copper salt. Barium chloride does not precipitate a barium salt from

aqueous solutions of the acid. The acid was not precipitated by phosphotungstic acid, but potassio-bismuth iodide gave a yellow, granular precipitate.

Solubility in Water at 30°.—One hundred parts water dissolved

I.	II.
0.3566 part acid	0.4038 part acid

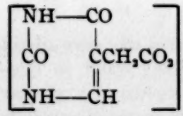
The Potassium Salt,  —This salt was very soluble in water and was prepared by dissolving the acid in water containing the required amount of potassium hydroxide. It crystallized from a concentrated aqueous solution in prismatic crystals containing water of crystallization. The water was determined by heating for one and a half hours at 105°–115°.

0.8947 gram substance lost 0.0307 gram H_2O.

	Calculated for $C_6H_6O_4N_2K.\frac{1}{2}H_2O$.	Found.
H_2O	4.1	3.45

Nitrogen determination in the anhydrous salt (Kjeldahl):

	Calculated for $C_6H_5O_4N_2K$.	Found. I.	Found. II.
N	13.45	13.58	13.47

The Lead Salt,  This was a very characteristic salt and separated, at once, when lead acetate was added to a hot, saturated, aqueous solution of thymine-5′-carboxylic acid. It was more insoluble than the acid and crystallized from boiling water in rhombic tables. It contained water of crystallization, which was determined by heating for two hours at 110°–115°.

0.3103 gram salt lost 0.0122 gram H_2O.

	Calculated for $(C_6H_6O_4N_2)_2Pb.H_2O$.	Calculated for $(C_6H_6O_4N_2)_2Pb.1\frac{1}{2}H_2O$.	Found.
H_2O	3.19	4.6	3.93

Nitrogen determination in the anhydrous salt (Kjeldahl):

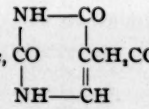
	Calculated for $(C_6H_6O_4N_2)_2Pb$.	Found.
N	10.28	10.32

Action of 20 Per Cent Sulphuric Acid on Thymine-5'-carboxylic Acid.—One gram of the acid was heated with 10 cc. of sulphuric acid for two hours, at 150°–160°. There was no pressure when the tube was opened and the acid had crystallized from the acid solution in prismatic crystals. They melted at 315°–320°, with decomposition, and when mixed with thymine the decomposition point was lowered below 300°. Analysis (Kjeldahl):

	Calculated for $C_6H_6O_4N_2$.	Found. I.	Found. II.
N	16.47	16.5	16.6

In a second experiment, 3 grams of thymine-5'-carboxylic acid were heated with 30 cc. of 20 per cent sulphuric acid for ten hours, at 160°–170°. We observed practically no decomposition under these conditions and the acid was recovered unaltered, melting at 315°–320°. Analysis (Kjeldahl):

	Calculated for $C_6H_6O_4N_2$.	Found.
N	16.47	16.35

Thymine-5'-ethylcarboxylate,  , was prepared in the usual manner by esterifying the acid with absolute alcohol and concentrated sulphuric acid. It crystallized from boiling alcohol in rectangular plates melting at 204°–210°, according to the rate of heating. Analysis (Kjeldahl):

	Calculated for $C_8H_{10}O_4N_2$.	Found. I.	Found. II.
N	14.14	13.7	13.9

NEW HAVEN, CONN.,
July 4, 1907.

CLI.—ON SOME DOUBLE AND TRIPLE SALTS OF CAESIUM NITRITE WITH NITRITES OF SILVER, THE ALKALI EARTHS, AND LEAD.

By George S. Jamieson.

The object of this work, primarily, was to investigate the possible triple salts of caesium and silver in combination with the alkali earth metals and lead.

Before attempting the investigation of the triple salts, a study of the double salts was made.

Since 1886, when Th. Rosenbladt[1] described the caesium and rubidium cobaltic nitrites, no one has attempted to make a study of caesium double nitrites, so far as could be ascertained from the literature. The double salts to be described are as follows:

$CsAg(NO_2)_2$,
$CsBa_2(NO_2)_5$,
$Cs_2Ba(NO_2)_4.H_2O$,
$Cs_2Ca(NO_2)_4.H_2O$,
$CsSr(NO_2)_3.H_2O$,
$CsPb(NO_2)_3.H_2O$.

The existence of two caesium barium salts is interesting, since barium generally shows little tendency to form double salts.

The following triple salts were obtained:

$Cs_3AgBa(NO_2)_6.2H_2O$,
$Cs_3AgSr(NO_2)_6.2H_2O$,
$Cs_3AgPb(NO_2)_6.2H_2O$,
$K_3AgPb(NO_2)_6.2H_2O$.

It is to be observed that all of these triple salts are analogous but that they do not correspond in type to any of the triple thiocyanates previously known, which have been prepared in this laboratory.[2] It was not possible to isolate a calcium triple salt of definite composition.

Many attempts were made to get a silver barium nitrite

[1] Ber. d. chem. Ges., **19**, 2531.

[2] See H. L. Wells: This Journal, **28**, 245 (1902); **30**, 144, 184 (1903).

as well as a silver strontium nitrite, but without success. A barium silver nitrite is described in Dammer 2^2, 806, but no references are given and none could be found in the literature. It was observed that the alkali earth nitrites tended to prevent the solution of silver nitrite.

EXPERIMENTAL PART.

Caesium Nitrite.—One hundred and fifty grams of caesium chloride, dissolved in about 200 cc. of hot water, were added to a solution which contained 137.1 grams of silver nitrite. The solution was thoroughly agitated, to facilitate the precipitation of the silver chloride. Then the solution was filtered and the filtrate was cautiously evaporated to a thick syrup. It is very essential that the silver nitrite should be in solution before adding the caesium chloride, otherwise the silver chloride formed coats over the nitrite and prevents further reaction.

Caesium nitrite was obtained in a crystalline form, from a very concentrated solution. It has a pale-yellow color and is anhydrous. The crystals were poorly developed. They were glassy in appearance and had a high index of refraction. The larger part of the material showed no distinct crystallization, but some of it, under the microscope, looked like octahedrons.

Caesium Silver Nitrite.—One molecule of silver nitrite (4.3 grams) was added to a hot solution which contained 10 molecules of caesium nitrite (50 grams). When the silver nitrite had dissolved, the solution was filtered and allowed to stand at room temperature overnight. It deposited sheets of hemimorphic needles, which were of a bright lemon-yellow color. The crystals were filtered by suction and pressed upon filter paper until dry. Cold water was found to decompose these crystals, causing them to become opaque. Four crops of this salt were obtained under different conditions. It was formed until the concentration of the silver nitrite reached 4 molecules, then silver nitrite separated. The various crops of crystals, by analysis, gave the following results:

	Calculated for $CsAg(NO_3)_2$.	Found. I.	II.	III.
$AgNO_3$	46.24	45.53	45.74	46.18
$CsNO_2$	53.76	54.23	54.13	53.82(Diff.)

Caesium Barium Nitrite.—This salt was only obtained when the concentration of caesium nitrite varied from 6–7 molecules to 10 molecules of barium nitrite.

Fifty grams of barium nitrite (10 mols.) and 23.4 grams of caesium nitrite (6 mols.) were dissolved in about 50 cc. water. The solution was kept at 0° during the night. Colorless, slender, rectangular prisms, which varied in length from 1 cm. to 1.5 cm., were obtained. The concentration of the caesium nitrite was increased to 7 molecules and another crop of the salt was formed. The salt is soluble in water. The following analyses were made of the two crops:

	Calculated for $CsBa_2(NO_3)_5$.	Found. I.	II.
$Ba(NO_3)_2$	71.90	71.51	71.84
$CsNO_3$	28.10	28.57	28.01

Caesium Barium Nitrite, $Cs_2Ba(NO_2)_4.H_2O$.—Another molecule of caesium nitrite was added to the above solution, which was again cooled to zero. Long, silky, colorless, hair-like crystals separated. These were found to be very soluble in water. This salt was obtained from a wide range of concentrations, which varied from 8–30 molecules of caesium nitrite to 10 of barium nitrite. The following analyses were made:

	Calculated for $Cs_2Ba(NO_2)_4.H_2O$.	Found. I.	II.	III.
$CsNO_2$	59.18	59.19	59.82	59.83
$Ba(NO_2)_2$	37.86	38.16	36.82	.....
H_2O	2.96	.....	3.14	.....

Caesium Silver-Barium Nitrite.—This salt was first obtained from a very concentrated solution, which contained 40 grams of caesium nitrite, 60 grams barium nitrite, and 15 grams of silver nitrite. The solution was warmed upon the steam bath until the silver nitrite was dissolved. The light orange-colored solution slowly deposited orange-yellow, needle-like prisms. In order to get another crop of the salt, a gram of silver nitrite and 5 grams of caesium nitrite had to be added

to the solution. By the addition of small quantities of silver and caesium nitrites, the triple salt was repeatedly obtained. Two crops of crystals gave, upon analysis:

	Calculated for $Cs_2AgBa(NO_2)_6.2H_2O$.	Found. I.	Found. II.
$AgNO_2$	16.10	15.42	15.13
$Ba(NO_2)_2$	23.95	25.54	25.20
$CsNO_2$	56.17	56.00	56.16
H_2O	3.76	3.18	....

The salt is decomposed by cold water.

Caesium Calcium Nitrite.—This salt was obtained from a concentrated solution in which there were 10 molecular proportions of calcium nitrite to 3 or 4 molecular proportions of caesium nitrite. It crystallized in hard, short, colorless prisms of microscopical size. The water of crystallization was driven off only at a rather high temperature. Analyses of two crops gave:

	Calculated for $Cs_2Ca(NO_2)_4.H_2O$.	Found. I. (a)	Found. I. (b)	Found. II.
$CsNO_2$	70.47	68.29	68.21	70.82
$Ca(NO_2)_2$	25.98	25.91	.....	25.77
H_2O	3.54	.....	.....	3.41 (Diff.)

Caesium Strontium Nitrite.—The salt was obtained from a concentrated solution which contained 10 molecules of strontium nitrite and 4 molecules of caesium nitrite. It separated in hemimorphic sheets of needles. It gave, upon analysis:

	Calculated for $CsSr(NO_2)_3.H_2O$.	Found.
$CsNO_2$	47.53	47.41
$Sr(NO_2)_2$	47.66	47.01 (Diff.)
H_2O	4.80	5.58

Although this appears to be a perfectly definite compound, many attempts to prepare another crop of it have failed.

Caesium Strontium-Silver Nitrite.—This salt crystallized in glistening, lemon-yellow, flat prisms, from a concentrated solution, which contained 10 molecules of strontium nitrite, 5 molecules of caesium nitrite, and all the silver nitrite that would remain dissolved at ordinary temperature. Several

crops were obtained by adding silver nitrite to the filtrates. The salt is partially decomposed by water, just like the barium triple salt. The analysis gave:

	Calculated for $Cs_2AgSr(NO_2)_4.2H_2O$.	Found. I.	II.
$CsNO_2$	59.23	57.56	57.51
$AgNO_2$	16.99	15.31	15.58
$Sr(NO_2)_2$	19.81	24.20	23.85
H_2O	3.97	2.93(Diff.)	4.06

Several other crops of crystals were obtained, but they contained one per cent less of silver nitrite and a correspondingly larger amount of the strontium nitrite. It was very difficult to separate the crystals from the syrupy mother liquors and dry them, and this fact doubtless accounts for the variations from theory in the analyses.

Caesium Lead Nitrite.—Five grams of caesium nitrite and 5 grams of lead acetate were dissolved in 20 cc. water by the aid of heat. Upon cooling the solution, bright, orange-colored plates separated. This salt is formed immediately upon mixing the constituents, as in the case of the analogous potassium lead nitrite.[1] The salt dissolved in cold water without decomposition, but when the solution was heated, some basic lead salt separated. The material, upon analysis, gave:

	Calculated for $CsPb(NO_2)_3.H_2O$.	Found. I.	II.
$Pb(NO_2)_2$	60.50	58.72	59.18
$CsNO_2$	35.85	37.25	.....
H_2O	3.65	4.03	.....

Caesium Silver-Lead Nitrite.—Three grams of the double caesium lead nitrite were dissolved in about 15 cc. of water, which contained 5 grams of caesium nitrite. The solution was heated and a gram of silver nitrite was added. When the solution became cool, a crop of bright-yellow, minute prisms separated. These appeared, under the microscope, to be rectangular. The crystals were filtered and some more silver nitrite was added to the filtrate, and another crop of the triple salt was obtained. The two crops gave the following analyses:

[1] Fischer: Pogg. Ann., 74, 105 (1848). Lang: *Ibid.*, 118, 282 (1863).

	Calculated for $Cs_2AgPb(NO_2)_6.2H_2O$.	Found. I.	II.
$CsNO_2$	52.34	51.99	.....
$AgNO_2$	15.01	15.48	15.79
$Pb(NO_2)_2$	29.15	29.05	29.12
H_2O	3.50	3.48	.....

Potassium Silver-Lead Nitrite.—Twenty grams of lead-potassium nitrite were dissolved in a solution which contained 20 grams of potassium nitrite. Then about 3 grams of silver nitrite were added to the hot solution. The solution deposited radiating bunches of yellow needles. These were filtered by suction and pressed dry on filter paper. The material analyzed as follows:

	Calculated for $K_2AgPb(NO_2)_6.2H_2O$.	Found. I.	II.
KNO_2	34.33	35.36(Diff.)	.....
$AgNO_2$	20.68	19.30	21.96
$Pb(NO_2)_2$	40.16	40.44	40.45
H_2O	4.83	4.90	.....

My thanks are due to Professor H. L. Wells for his valuable suggestions and for the use of the caesium material.

SHEFFIELD SCIENTIFIC SCHOOL,
NEW HAVEN, CONN.,
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Contributions from the New York Agricultural Experiment Station.

XII.—THE HYDROLYSIS OF THE SODIUM SALTS OF CASEIN.

BY LUCIUS L. VAN SLYKE AND DONALD D. VAN SLYKE.

In determining the amount of alkali that is neutralized by casein, the results obtained by the use of different indicators do not agree. Thus more alkali is required with litmus than with methyl orange, and still more with phenolphthalein.[1] The amount of alkali which casein neutralizes, with the use of phenolphthalein as indicator, has been chosen somewhat arbitrarily as representing the true result. It was on the basis

[1] Söldner: Landw. Vers. Stat., **35**, 351 (1888). Courant: Arch. Physiol. (Pflüger), **50**, 109 (1891). Laqueur: Beitr. chem. Physiol. u. Path., **7**, 273 (1905).

of results thus obtained that Laqueur and Sackur[1] made their determination of the equivalent weight of casein.

The desirability of a method of measuring the neutral point, in such cases, independently of indicators, is apparent. It was hoped that the determination of electrical conductivity would furnish this. It is well known that when an acid is added to a solution of a strong base, the conductivity of the solution decreases until the neutral point is reached, because the addition of acid replaces rapidly conducting OH' ions with more slowly conducting acid radicle anions. The addition of a given amount of acid replaces the same number of OH' ions and decreases the conductivity by a certain amount. Therefore, if the conductivities are plotted as ordinates and the amounts of acid added, volume of solution being constant, as abscissae, the resulting curve will be a straight line sloping downward to the neutral point, at which it breaks sharply.

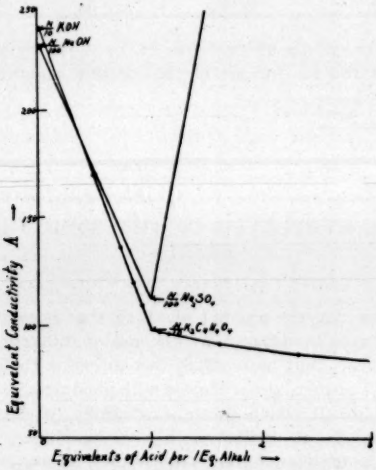


Fig. I.

[1] Beitr. chem. Physiol. u. Path., **3**, 197 (1903).

If the acid is a strong one, like sulphuric acid (Fig. I.), the curve will rise again rapidly in a nearly straight line. If the acid is a weak polybasic one, like succinic (Fig. I., lower curve), the curve may still continue falling slightly on the acid side of the neutral point, due to the fact that the acid salt has somewhat lower conductivity than the neutral salt, but the slope is slight compared with that on the alkaline side of the neutral point, which is plainly marked by a sharp angle. If the acid is so weak, however, that it hydrolyzes, so that its normal salt reacts alkaline, as is the case with phosphoric acid, the curve does not fall straight to the neutral point and break there, but bends gradually (H_3PO_4, Fig. II.) and without break-

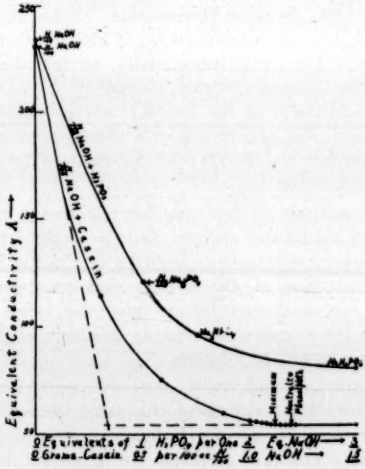


Fig. II.

ing. The decrease in the number of OH' ions is not a linear, but a complex, function of the amount of acid added, and they do not disappear until an excess of acid has been added. In acids of this character, the neutral point can not be determined accurately by

either conductivity or titration with phenolphthalein. Sjöqvist,[1] working with hydrolyzible hydrochloric acid salts of albumin, employed the approximate method of determining the intersection of the asymptote of the curve on the acid side (corresponding to the alkaline in our case), with the horizontal line tangent to the curve at its minimum, assuming that the abscissa of the intersection denoted the equivalent weight of albumin.

The work of former investigators has shown that the addition of more casein to a sodium caseinate solution neutral to phenolphthalein does not appreciably change the conductivity. The curve instead of rising beyond the neutral point, as in the case of sulphuric acid, or falling slightly, as in the case of succinic acid, becomes horizontal. If an acid sodium salt of casein, analogous to $NaHCO_3$, is formed, this acid salt has apparently the same conductivity as the neutral salt. Apparently, the $(H\text{-casein})^{n-1}$, $(H_2\text{-casein})^{n-2}$.....ions have the same conductivity as the $(casein)^n$ ion (n equals valence of casein anion), the gain or loss of a hydrogen atom not appreciably affecting the velocity of the excessively large and complex casein anion.

Laqueur[2] mentions the fact that increase in the proportion of casein in a solution of sodium caseinate neutral to phenolphthalein does not appear to change the conductivity so long as the concentration of the sodium remains constant, and discusses the explanation mentioned above; also, as less probable, the one that the excess casein simply dissolves as free casein in the sodium caseinate solution.

The constant conductivity of solutions, neutral or acid to phenolphthalein but containing the same concentration of sodium, is shown more accurately by the figures of Long,[3] although he does not call attention to this feature. Rearranging Long's results so as to make this point clear, we have the following table:

[1] Skand. Arch. Physiol., **5**, 276 (1895).
[2] Beitr. chem. Physiol. u. Pathol., **7**, 273 (1903).
[3] J. Am. Chem. Soc., **28**, 377 (1906).

Cc. N/10 NaOH in 100 cc.	Grams casein.	Conductivity × 10^6.	Reaction to phenolphthalein.
22.50	1.25	1234	alkaline
	2.5	1006	neutral
	5.0	1012	acid
11.25	0.625	700	alkaline
	1.25	561	neutral
	2.50	563	acid
5.625	0.3125	380	alkaline
	0.625	310	neutral
	1.25	308	acid
2.812	0.1562	209	alkaline
	0.3125	172	neutral
	0.625	168	acid
1.406	0.1562	93	neutral
	0.3125	93	acid

The last two figures of each trio in the conductivity column agree closely.

From the preceding discussion, it is apparent that if casein acts as an acid with a definite neutral point correctly indicated by phenolphthalein, as was apparently considered to be approximately the case by Laqueur and Sackur,[1] who based equivalent- and molecular-weight determinations upon this assumption, we should expect a neutralization conductivity curve descending in a straight line to the neutral point and then breaking and becoming horizontal.

The curve actually obtained (Fig. II.) is concave and gradually approaches the horizontal position without the occurrence of a break at any point. The curve reaches its minimum at a point near that neutral to phenolphthalein, but it does not appear that this point indicates the normal salt any more than the minimum on the phosphoric acid curve indicates the salt Na_3PO_4. It indicates, rather, the presence of sufficient excess of casein to depress the amount of hydrolytically freed alkali to a negligible quantity. If we adopt Sjöqvist's method and extend the asymptote of the upper part of the curve until it cuts the horizontal line tangent at the minimum (see dashed lines in Fig. II), the intersection indicates an equivalent weight of casein less than one-third that estimated from the point neutral to phenolphthalein. The assumption of Laqueur and

[1] Beitr. chem. Physiol. u. Pathol., **3**, 193 (1903).

Sackur, that the latter indicates approximately the true equivalent weight of casein, is not confirmed. It does not appear that this can be ascertained by titration with acid-alkali indicators any more than can that of phosphoric acid, although as applied by Robertson[1] it may furnish the basis of a convenient empirical method for quantitative estimation of the proteid.

Experimental.

We dissolved varying amounts of casein in 100 cc. of N/100 NaOH and determined the point of minimum conductivity by the method of repeated approximation, finding the point within wide limits, then working within these limits and finding narrower limits, etc. The methods of manipulation in agitating casein with alkali and in measuring conductivities were the same as in the case of acids.[2] The solutions were thus in contact with the electrodes only a short time, avoiding chances of the difficulty mentioned by Laqueur.[3]

We obtained the following results, graphically expressed in Fig. II., using in each case 100 cc. of N/100 NaOH with the amounts of casein indicated.

Grams of casein.	Equivalent conductivity. Λ.	Per cent free NaOH by conductivity.	Color of solution with phenolphthalein.
0	232.0	100.00	red
0.291	114.0	33.55	"
(0.335)	(106.0)	(29.05)	"
0.581	75.7	12.00	"
0.872	59.7	2.98	"
1.000	56.2	1.01	"
1.030	55.4	0.56	"
1.060	55.1	0.39	"
1.080	54.9	0.28	"
1.100	54.7	0.17	"
1.120	54.4	0.00	"
1.140	54.3	"	"
1.160	54.4	"	"
1.180	54.3	"	"
1.200	54.3	"	slightly pink
1.500	54.4	"	colorless
1.800	54.4	"	"

[1] Jour. Biol. Chem., 2, 317 (1907).
[2] This Journal, 28, 391 (1907).
[3] Beitr. chem. Physiol. u. Pathol., 7, 275 (1906).

The numbers in parentheses are graphically interpolated from the curve and correspond to the point indicating the normal salt, according to Sjöqvist's roughly approximate method. This normal salt, with no excess of casein present, appears to be about 29 per cent hydrolyzed. The free alkali in the data tabulated below this in the column may be regarded as all due to hydrolysis.

The per cent of free NaOH in the third column is calculated by the formula usually employed for hydrolysis, $k_1x + (1-x)k_2 = k_3$; $100x$ equals per cent of free alkali; k_1 indicates conductivity of free alkali (= 232); k_2 indicates conductivity of unhydrolyzed sodium caseinate (= 54.4); k_3 indicates observed conductivity of experimental solution. The accuracy of the formula depends on that of the observation, brought out previously, that the equivalent conductivities of the neutral and various acid sodium salts of casein are the same.

The view that the sodium salts of casein hydrolyze was held by Laqueur and Sackur[1] for the salts acid to phenolphthalein. Our results indicate that the salts even quite alkaline to phenolphthalein hydrolyze to a marked degree. The behavior of casein salts of the alkaline earth metals also has been studied by W. A. Osborne,[2] with the conclusion that they hydrolyze.

A further reason for placing casein, as regards its acid properties, in a class with phosphoric acid is the similar behavior of the two towards various indicators. Phosphoric acid, like casein, gives different results when titrated against alkali with different indicators. For example, 10 cc. of a given solution of phosphoric acid was neutralized to methyl orange by 6.15 cc. N/10 KOH, while, to give a perceptible pink with phenolphthalein, 11.20 cc. were required.

Viewed from the standpoint indicated by our results, casein acts as a very weak acid. When a sufficient excess of casein is present in solution (presumably as acid casein salts, possibly as free casein dissolved in sodium caseinate solution), the amount of hydrolytically freed alkali is reduced to practically zero, and the solution reacts neutral to the delicate indicator

[1] Beitr. chem. Physiol. u. Pathol., **3**, 191 (1903).
[2] Jour. Physiol., **27**, 398 (1901).

phenolphthalein, at the same time showing a minimum conductivity. Owing to the weakness of its acid properties, a considerably greater excess of casein is required to render the solution acid enough to redden litmus, and still greater excess to neutralize methyl orange.

These results are presented as preliminary to a more thorough investigation of the problem.

The data for plotting the phosphoric acid and sulphuric acid curves are taken from Kohlrausch.[1] The data for succinic acid were obtained by adding to a solution of 20 cc. carbonate-free N/10 potassiuim hydroxide, in a conductivity cell, successive portions of recrystallized succinic acid dried at 115°. The acid was weighed out in a small tube and portions shaken into the solution, the tube being weighed after shaking out each portion. By this method, cumulative error in weighing was avoided. As one equivalent of succinic acid weighed only 116 milligrams, the volume change caused by this addition was negligible. The following data were obtained at a temperature of 25°.

Equivalents succinic acid added.	A.
0	240.0
0.5008	171.7
0.7231	138.0
0.8405	121.4
0.9137	111.6
0.9835	102.0
1.043	99.1
1.149	97.8
1.614	93.1
2.331	88.7
3.100	86.2

For courtesy in providing us with apparatus, laboratory conveniences, and materials for the work described above with succinic acid at a time when our own apparatus was not available, we wish to thank Dr. Lind, of the University of Michigan.

[1] Leitvermögen der Elektrolyte.

ON THE BASE-FORMING PROPERTY OF CARBON.

By James F. Norris.

Some time ago Norris and Sanders[1] described a compound of triphenylchlormethane and aluminium chloride of the formula $(C_6H_5)_3CCl.AlCl_3$, and drew attention to the fact that the substance, which was the first compound of an alkyl chloride with a metallic chloride to be prepared, resembled an inorganic double halide. Kehrmann[2] immediately prepared other double salts containing triphenylchlormethane. The existence of such substances led to the conception that triphenylchlormethane and analogous compounds were true salts, and that the methane carbon in these compounds had weakly base-forming properties. In discussing this view the following statement in regard to triphenylcarbinol was made in a paper by Norris and Franklin published in 1903.[3] "The compound resembles to some extent the hydroxides of certain elements which are in the borderland between the well-defined acid- and base-forming elements. It is probable that by a change in the nature of the radicals, the basic property of the compound can be increased to such an extent that a true carbon base will be produced." It was the intention of the writer to put this suggestion to the test immediately, but it was found inadvisable to continue the work until recently.

In the meantime Baeyer,[4] in following out the similarity between the double compounds of triphenylchlormethane and those of inorganic salts, was led to investigate a number of tertiary aromatic alcohols and their derivatives. Among the compounds prepared were certain sulphates which were highly colored. The result of his work was the proposal of his carbonium theory, and its application to the explanation of the structure of the triphenylmethane dyes.

The work about to be described was undertaken with the object of testing the suggestion quoted above. The systematic study of the problem involved the preparation of a number

[1] This Journal, **25**, 54.
[2] Ber. d. chem. Ges., **34**, 3815.
[3] This Journal, **29**, 141.
[4] Ber. d. chem. Ges., **38**, 569.

of aromatic alcohols, and an investigation of their relative basicity. The most characteristic property of bases is their power to form salts with aqueous solutions of acids. The alcohols studied were, accordingly, tested to determine whether they possessed this property. An approximate notion of the relative basicity of a number of compounds was formed by determining the relation between the lowest concentrations of the aqueous solutions of a certain acid by means of which the various compounds could be converted into salts.

In this paper the results obtained in the study of the action of aqueous solutions of hydrochloric and hydrobromic acids on benzyl alcohol, and diphenyl-, triphenyl-, and tritolylcarbinols are described. As it was found in certain cases that the formation of salts took place readily, the action of aqueous solutions of hydrochloric, hydrobromic, and hydriodic acids on certain monatomic alcohols of the fatty series was investigated.

When triphenylcarbinol is treated with hydrochloric acid (sp. gr. 1.20) it is converted quantitatively, in the cold, into triphenylmethyl chloride. As both the carbinol and the chloride are almost insoluble in the acid, it is necessary to have the carbinol in a finely divided condition in order to get complete reaction. This can be accomplished by grinding the alcohol with the acid in a mortar, or, better, by adding slowly to the acid a solution of the carbinol in some solvent which mixes with water, for example, acetic acid, acetone, or alcohol. Triphenylmethyl bromide and iodide are formed in the same way when hydrobromic acid (sp. gr. 1.49) and hydriodic acid (sp. gr. 1.7) are used.

As the study of *p p' p''*-tritolylcarbinol brought out the fact that its basicity was greater than that of the analogous phenyl compound, the reactions of the former were studied in greater detail. Dilute hydrochloric acid (sp. gr. 1.12) converts tritolylcarbinol into the chloride, whereas an analogous transformation does not take place in the case of triphenylcarbinol with acid of this strength. The greater basicity of the tolyl compound is also shown by the fact that it reacts with nitric acid (sp. gr. 1.42) and gives a nitrate, which appears to have

the formula $(CH_3C_6H_4)_3CNO_3.2HNO_3$. Under the same conditions triphenylcarbinol is not changed. The latter substance dissolves in fuming nitric acid, and is precipitated unchanged by the cautious addition of water.

Triphenylcarbinol dissolves in concentrated sulphuric acid, and, in all probability, forms a sulphate. When even a small quantity of water is added to the solution the carbinol is precipitated. Tritolylcarbinol, on the other hand, dissolves in a mixture of equal volumes of water and sulphuric acid. If the solution is saturated at the temperature of the steam bath and then placed in a freezing mixture, a sulphate of the composition $(CH_3C_6H_4)_3CSO_4H.H_2SO_4$ crystallizes out in silky needles. The salt has a deep orange color and resembles in properties and composition the sulphates prepared by Baeyer. It is, however, more stable. Baeyer's method of preparing the sulphates was to bring the carbinol and concentrated sulphuric acid together in an organic solvent. Chloral was used, as it united chemically with the water formed in the reaction. The sulphate was then precipitated by some dry organic liquid in which it was not soluble. These precautions are not necessary in the case of tritolylmethyl sulphate, on account of the greater basicity of the carbinol from which it is prepared.

From the above it appears that tritolylcarbinol reacts as a base, as it forms a chloride, bromide, iodide, nitrate, and sulphate with aqueous solutions of the respective acids. The base-forming property of carbon is not highly developed, however, as all these salts are formed only in relatively concentrated solutions of the acids, and all are hydrolyzed more or less readily by water. There is some analogy between the behavior of these salts and those of bismuth.

The reactions of the compounds prepared from tritolylcarbinol are strong evidence of their being true salts. A solution of tritolylmethyl chloride in acetone is a conductor of electricity. When a direct current is passed through such a solution, a red substance is deposited upon the cathode. This substance loses its color when brought in contact with air. It probably resembles in composition Gomberg's triphenylmethyl. This reaction is now under investigation. When

a solution of the chloride in acetone is treated with silver nitrate or silver sulphate, a metathesis takes place and silver chloride is precipitated.

Tritolylmethyl sulphate is the only salt so far prepared which dissolves in water, and in this case solution without decomposition is only possible in the presence of a large excess of acid. The solution prepared by dissolving the sulphate in sulphuric acid (one volume of water and one volume of acid), or by dissolving the carbinol in the same solvent, exhibits the characteristic properties of a solution of an inorganic salt. This is readily shown by adding to such a solution sodium chloride. Tritolylmethyl chloride, which is insoluble, is immediately precipitated. The reaction appears to be quantitative, and is similar to the precipitation of silver from its salts

Certain reactions of tritolylmethyl chloride and of tritolylmethylethyl ether are of interest in this connection. The chloride is decomposed by concentrated sulphuric acid at room temperature, the reaction being analogous to that between sodium chloride and the acid:

$$(CH_3C_6H_4)_3CCl + H_2SO = (CH_3C_6H_4)_3CSO_4H + HCl.$$

This reaction may be made to proceed in the opposite direction to that in which it is written by adding concentrated hydrochloric acid to a solution of the sulphate in sulphuric acid. The metathesis follows the laws which apply to such changes in inorganic chemistry.

Tritolylmethyl chloride reacts with alcohol in the presence of an excess of the latter, according to the following equation:

$$(CH_3C_6H_4)_3CCl + HOC_2H_5 = (CH_3C_6H_4)_3COC_2H_5 + HCl.$$

This is also a reversible reaction, for the ether is converted into the chloride when it is treated with a large excess of concentrated hydrochloric acid. The ether is also formed when a small quantity of hydrochloric acid is added to a solution of tritolylcarbinol in alcohol. The acid acts as a catalytic agent. It in all probability reacts with the carbinol to form the chloride, which, in turn, reacts with the alcohol to produce the ether and hydrochloric acid. The process is then repeated.

The action of acids on diphenylcarbinol was next studied, in order to determine whether the replacement of a phenyl group by hydrogen had a marked influence on the basicity of the compound. The carbinol was readily changed into a chloride and a bromide by concentrated solutions of hydrochloric and hydrobromic acids. In the same way benzyl chloride, bromide, and iodide were prepared from benzyl alcohol. In the case of this alcohol, gentle heat was applied in order to bring about the reaction quickly.

It is seen from the above that typical primary, secondary, and tertiary aromatic alcohols exhibit basic properties. A quantitative determination of the relative basicity of a number of such alcohols is now being made.

The fact that aromatic alcohols reacted so readily when treated with aqueous solutions of the halogen acids led to an investigation of the behavior of alcohols of the paraffin series under the same conditions. The chances of the replacement of the hydroxyl group by halogen taking place to any great extent seemed small, as those who have studied the action of halogen acids on alcohols have always endeavored to eliminate water in order to bring about the reaction. The usual method is to saturate the alcohol at a low temperature with the gaseous acid and to heat the mixture in a sealed tube at a comparatively high temperature, or to pass the gaseous acid into the boiling alcohol in the presence of fused zinc chloride.

As the replacement of the hydroxyl group by halogen is, in general, not satisfactorily accomplished in this way, the halogen compounds are usually prepared by the action of the halides of phosphorus on the alcohols—a method which often gives poor yields, as a number of side-reactions take place.

Tertiary butyl alcohol was first studied, as it seemed that its basic properties would be greater than those of a primary alcohol. Concentrated hydrochloric acid reacts with the alcohol in the cold, and a quantitative yield of tertiary butyl chloride is obtained. In the study of the action of hydrobromic and hydriodic acids on the alcohols, the most concentrated aqueous solutions were not used. It was found that the mixtures of the alcohols and acids required heating in most cases

to bring about reaction, and that under these conditions a large amount of the acids was lost. The constant-boiling mixtures of the acids and water were used, as solutions of the concentration of these mixtures effected the replacement of the hydroxyl group by bromine and iodine. When tertiary butyl alcohol was gently heated with hydrobromic and hydriodic acids, the bromide and iodide were obtained. When the alcohol and acid were mixed in the proportion of one molecular weight of the former to two of the latter the yields of the bromide and iodide were 91 per cent and 89 per cent of the theoretical, respectively.

When a mixture of secondary butyl alcohol and hydrobromic acid, in the molecular ratio of one of the former to three of the latter, was distilled, a yield of 95 per cent of the calculated amount of bromide was obtained. This result is of interest in light of the fact that Norris and Green[1] showed that secondary butyl alcohol was not converted into the bromide when hydrogen bromide was passed into the boiling alcohol which contained fused zinc chloride. A yield of 95 per cent of secondary butyl iodide was obtained when an aqueous solution of the halogen acid was used.

With hydrochloric acid the results were quite different in character. When a large excess of concentrated hydrochloric acid was used no chloride was obtained on distillation. The alcohol distilled unchanged with the acid. On account of this result a solution of hydrochloric acid was prepared which had the same molar concentration as the hydrobromic acid solution which gave a yield of 95 per cent of the bromide. A mixture of the alcohol and acid in the same proportions as used in the preparation of the bromide was distilled. The yield of chloride was 12 per cent. When the alcohol was distilled with a large excess of the constant-boiling mixture of hydrochloric acid and water, which mixture contains a larger percentage of water than the acid used in the experiment just noted, the yield of chloride was increased to 50 per cent. The alcohol which distilled unchanged was readily recovered by treating the aqueous part of the distillate

[1] This Journal, **36**, 293.

with a strong solution of potassium hydroxide. The recovered alcohol was returned to the distilling flask, and the distillation continued. As a result, the total yield of chloride was 72 per cent. The remarkable fact that the alcohol is converted into the chloride by dilute acid, whereas the concentrated acid does not effect this change, will be discussed farther on.

The conversion of a secondary alcohol into a chloride by distilling the former with an aqueous solution of hydrochloric acid is not a characteristic reaction of compounds of this class, as it was found impossible to prepare isopropyl chloride in this way. Isopropyl bromide and iodide were, however, prepared readily and good yields were obtained.

The primary alcohols studied were methyl, ethyl, propyl, isobutyl, isoamyl, and allyl alcohol. In all cases the alcohols were mixed with aqueous solutions of hydrobromic acid (sp. gr. 1.49) and hydriodic acid (sp. gr. 1.70) and slowly distilled. The effect on the yield of the halide of varying the molecular proportions of the reacting substances was studied in a number of cases. In general it was found that increase in the amount of acid produced larger yields. When the molecular ratio of one of the alcohol to three of the acid was used, the yields were satisfactory. For example, the yields of ethyl bromide, ethyl iodide, propyl bromide, and propyl iodide were 81, 84, 88, and 89 per cent, respectively.

This method of preparing the alkyl bromides and iodides is superior to any used in the past. The yields are excellent, and there is no loss of reagents. The alcohol which does not enter into reaction can be recovered by treating the aqueous distillate with potassium hydroxide, or the yield can be made almost that required by theory, by using a large excess of the solution of the acid. There is no loss of the latter. After the bromide or iodide has distilled over, the diluted acid which remains in the flask may be distilled slowly until its boiling point reaches that of the constant-boiling mixture of acid and water, when more alcohol may be added and the process repeated. The method is of particular value when a synthetic alcohol, requiring much time for its preparation, is to be converted into the corresponding bromide or iodide. When the

halides are prepared by means of the phosphorus compounds the yields are often small. The method is of value on account of its simplicity. The alcohol and acid are mixed and distilled. The halide and a small amount of water distil over at once. It is not necessary to distil the whole mixture.

Under no conditions were the primary alcohols converted into chlorides when distilled with aqueous solutions of hydrochloric acid. The results emphasize the well-known difference in the behavior of the halogen acids toward organic compounds.

From the facts stated above a conception of the relative basicity of the different classes of alcohols can be gained. The primary fatty alcohols are not converted into chlorides by hydrochloric acid. Some secondary alcohols are so converted at slightly elevated temperatures, while tertiary alcohols react with this reagent at room temperature. The temperature at which the members of a series of isomeric alcohols react with hydrobromic acid varies with the type of alcohol. For example, isobutyl alcohol reacts with hydrobromic acid at 105°, secondary butyl alcohol at 65°, and tertiary butyl alcohol at 35°.

The nature of the reaction which takes place in the replacement of an alcoholic hydroxyl group by halogen is not clear from the experimental results obtained as yet. It is evident, from the results of the study of the action of the alcohols on hydrochloric acid and on hydrobromic acid of the same molar concentration, that the reaction is not an ionic one. A number of facts indicate that the reaction may consist in the formation of an addition product of the halogen acid and alcohol, and the subsequent decomposition of this compound with the elimination of water. When the primary fatty alcohols are heated with hydrochloric acid, no chloride is formed, but the distillates appear, in some cases, to have definite boiling-points, and contain both the alcohol and hydrochloric acid. It has not yet been determined whether the distillates are compounds of the alcohols and the acid, or are of the nature of the constant-boiling mixtures of the acid and water. The fact that the lower fatty alcohols which are insoluble in water dissolve

readily in aqueous solutions of the halogen acids, is, perhaps, some evidence in favor of the view that addition products are formed.

As the reaction between an alcohol and a halogen acid is a reversible one, the decomposition of a halide by water consists, if the above view is correct, in the addition of water and the subsequent elimination of halogen hydride. The temperature is an important factor in determining the equilibrium in the system. The description of an experiment with tertiary butyl bromide will make this statement clear. About 25 grams of the bromide were allowed to stand with an equal volume of water. At the end of a few days, during which time the reacting substances were occasionally shaken, the bromide disappeared and a homogeneous liquid was formed. The mixture was divided into two portions. One of these was treated with potassium hydroxide and yielded the alcohol. When the other portion was heated, about one-half of the alcohol present was converted into the bromide. It follows that, if it is desired to decompose a halide with a small amount of water, the temperature of the reacting mixture must be below that at which the alcohol reacts with the acid, if a complete transformation is to take place.

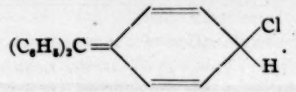
A satisfactory explanation of the mechanism of the replacement of a hydroxyl group in an aromatic alcohol by halogen is difficult to obtain, as the possibilities are greater than is the case with the fatty alcohols. This explanation must take into account the structure of the resulting halide, for example, triphenylchlormethane. Two striking views of the structure of this substance are before chemists. According to Baeyer the compounds formed by replacing the hydroxyl group in a tertiary aromatic alcohol by the halogens or the group SO_4H, may exist in two modifications, one of which has a structure analogous to that assigned to similar fatty compounds (formula 1).

(1) $(C_6H_5)_3C - Cl$ (2) $(C_6H_5)_3C \overset{\frown}{\smile} Cl$

In the other, the carbon atom possesses peculiar basic properties, and the compounds containing such carbon atoms are true salts. In order to represent this property graphically the form-

ula is written as above (2). The compounds are called carbonium salts. It has been found impossible up to the present to obtain in the free condition substances corresponding to formula (2), but according to Baeyer they exist in solution and in double salts. Substances containing the carbonium linking are highly colored. According to this view triphenylcarbinol has no basic properties, but is converted by acids into triphenylcarbonium hydroxide, which then reacts to form triphenylcarbonium chloride. The latter compound exists as such in certain solvents, but if an attempt is made to get the substance in the solid state, it changes into colorless triphenylchlormethane. Experiment shows that when colorless tritolylcarbinol is converted into colorless tritolylmethyl chloride, a colored intermediate product is formed.

The other important view is that of Kehrmann. According to this conception the colored compounds derived from triphenylchlormethane and similar substances, contain a quinoid grouping. The graphic symbol of the form of triphenylchlormethane which shows the properties of salts, and gives a color to the compounds in which it is present, is this:



The recent work of Gomberg and others on "triphenylmethyl" is evidence in favor of this view.

The experimental results obtained in this research are of interest in connection with the above views, although, as yet, they do not serve to answer the question as to the nature of the change which takes place in the replacement of hydroxyl by halogen. A number of the chemical properties of tertiary butyl alcohol are like those of triphenylcarbinol. Both substances are converted by concentrated hydrochloric acid into chlorides which are decomposed by water. Both react with acetyl chloride and form, not an acetate, as is usual, but a chloride. The bromides of the two alcohols react with ethyl alcohol, and hydrogen bromide is set free. The acid is also

formed when the bromides are treated with concentrated sulphuric acid. In view of this similarity in behavior in a number of chemical reactions, it is probable that the basicity of the triphenylmethyl and the tertiary butyl groups are of the same order of magnitude, and that the reactions of the two substances with acids would be of the same nature. The formation of a carbonium compound of tertiary butyl might, accordingly, be expected. When the two alcohols are treated with hydrochloric acid, chlorides are formed, but the striking fact appears that, during the transformation, a marked yellow color is produced in the case of the aromatic alcohol, whereas no color is evident when the fatty compound is used. This difference is readily explained if we accept the quinoid formula for the colored compounds.

There are other possible explanations which must be studied before a conclusion can be reached as to the nature of the colored compounds. They may be oxonium salts, or the existence of color may be associated with formation of complex molecules when the so-called partial valences come into play. An attempt will be made to collect evidence bearing upon this latter view. An effort will also be made to prepare a carbinol having greater basic properties than those of tritolylcarbinol.

EXPERIMENTAL.

In this section will be given some details of the experimental work not described above.

Tritolylmethyl Nitrate.—Nitric acid, of the specific gravity 1.42, reacts with *pp'p''*-tritolylcarbinol at room temperature. The colorless crystals of the carbinol are changed into a red oil, which floats on the acid. For analysis the oil was separated from the acid by rotating a tube containing the mixture in a centrifuge. The upper layer was separated by means of a pipette. The substance was analyzed by determining the amount of acid formed when it was hydrolyzed by water into nitric acid and tritolylcarbinol. The salt was decomposed by heating it with water, or a solution of it in acetone was poured into water, when the hydrolysis took place at once. A number of analyses were made, as it was found that the per-

centage of nitric acid found varied with different samples. It was impossible to free the salt from small amounts of nitric acid mechanically held. The percentages of nitric acid obtained varied between 39.11 and 43.60 per cent. The theory for the formula $(CH_3C_6H_4)_3CNO_3.2HNO_3$ is 39.96 per cent. The oil loses nitric acid slowly in the air, more rapidly in a desiccator over potassium hydroxide, and when heated at 100° about two-thirds of the acid is quickly lost.

Tritolylmethyl Sulphate.—Equal weights of tritolylcarbinol and concentrated sulphuric acid were warmed together on the steam bath. On cooling, an orange-colored crystalline mass was formed. This was dissolved, by heating on the steam bath, in a mixture of equal volumes of concentrated sulphuric acid and water. The solution was then placed in a freezing mixture, and the crystals which separated were dried on a porous tile which had been previously cooled. As the salt is readily decomposed by water, it is necessary to keep it in a desiccator over sulphuric acid. The salt was analyzed by determining the sulphuric acid formed when it was decomposed by water into the carbinol and acid. The percentage of sulphuric acid found was 40.61; the calculated for $(CH_3C_6H_4)_3CSO_4H.HSO_4$ is 40.84 per cent.

Some tritolylcarbinol was dissolved in sulphuric acid (sp. gr. 1.5) and to the solution was added some finely powdered sodium chloride. The precipitate which formed immediately was shown to be tritolylmethyl chloride. As the filtrate when added to water gave no precipitate, it was evident that the tritolylmethyl group had been completely precipitated as chloride. Concentrated hydrochloric acid, when added to the solution of the sulphate, also caused the precipitation of the chloride.

Benzyl Chloride.—Two grams of benzyl alcohol and 6 grams of concentrated hydrochloric acid were mixed and slowly heated. At 60° the mixture separated into two layers. The yield of benzyl chloride was 70 per cent of the theoretical. When the alcohol and a large excess of the acid were mixed, the reaction took place at the room temperature after a few minutes, and a theoretical yield of the chloride separated. Benzyl alcohol dissolves sparingly in hydrochloric acid of the specific

gravity 1.12. When the solution is warmed, benzyl chloride is formed. Benzyl bromide and iodide were prepared in the same way from the corresponding acids.

Preparation of the Alkyl Halides.—The method of preparing the bromides and iodides was as follows: A mixture of the alcohol and the acid was slowly distilled. The weight of alcohol used varied in different experiments from 5 to 20 grams. The acids used were hydrobromic acid of the specific gravity 1.49 and hydriodic acid of the specific gravity 1.70. In order to find out at what temperature the reaction began, the distilling flask was fitted with a thermometer, the bulb of which was in the liquid. The temperature of the liquid was noted when there was the first evidence of the formation of the organic halide. In some cases this was shown by the condensation of the halide in the neck of the flask; in some cases the liquid clouded as a result of the sudden formation of the halide. The determination of the temperature in this way was an approximation only. The halide distilled over first. Toward the end of the reaction some dilute acid passed over with the halide. The products were shaken with concentrated hydrochloric acid to remove any alcohol which had distilled unchanged. The yields given below are those calculated from the specific gravity and the volumes of the halides after they were washed. In all cases the products were dried and distilled and found to be pure. A brief statement about each experiment follows.

Methyl Bromide.—Five grams of methyl alcohol were distilled with 79 grams of hydrobromic acid (molecular ratio, 1 of alcohol to 3 of acid). The bromide was condensed by passing the gas into a cylinder containing hydrochloric acid and surrounded by a freezing mixture. The yield was 7.3 grams, which is 50 per cent of the theoretical.

Methyl Iodide.—Five and one-half grams of methyl alcohol and 105 grams of hydriodic acid gave 21 grams of methyl iodide, a yield of 86 per cent. The reaction appeared to begin at 70°. When about one-half of the iodide had distilled over, the aqueous distillate measured 0.5 cc. When the reaction was complete the latter measured 2 cc.

Ethyl Bromide.—When the mixtures which were distilled contained the alcohol and the acid in the molecular ratio 1 to 3, 1 to 3.5, and 1 to 4, the yields were 71, 81, and 86 per cent, respectively. The reaction between the alcohol and acid began at about 90°.

Ethyl Iodide.—Ten grams of alcohol and 147 grams of hydriodic acid (molecular ratio, 1 to 3) gave 27 grams of the iodide, which is 84 per cent of the theoretical. The reaction began at about 85°. An experiment was made to determine the effect upon the yield of a large excess of alcohol. When the molecular ratio was 3 of alcohol to 1 of acid, the yield was 53 per cent of the theoretical amount calculated from the acid.

n-Propyl Bromide.—When the alcohol and acid were in the molecular ratio of 1 to 2, respectively, the yield of bromide was 59 per cent. With 4 parts of acid this was increased to 84 percent.

n-Propyl Iodide.—The reaction began at 86°. When the ratio of alcohol to acid was 1 to 3, the yield was 87 per cent.

Isopropyl Bromide.—Ten grams of the alcohol and 84 grams of the acid (molecular ratio, 1 to 3) gave 18 grams of the bromide, a yield of 89 per cent.

Isopropyl Iodide.—When the ratio was 1 to 2 the yield was 89 per cent. Reaction started at about 70°.

Isobutyl Bromide.—Experiment with this alcohol showed that the rate of distillation had a marked effect upon the yield of halide. Two experiments were carried out with mixtures containing the alcohol and acid in the ratio of 1 to 3. When the mixture was distilled as rapidly as possible, the yield was 30 per cent. With slow distillation this was increased to 55 per cent. The reaction began at about 105°.

Isobutyl Iodide.—In this case the yield was not so good as with the other alcohols. The reaction began at about 100° when the ratio was 1 to 3. The yield of iodide was 64 per cent.

Secondary Butyl Bromide and Iodide.—When the ratio was 1 of alcohol to 3 of acid, the yield of both bromide and iodide was 95 per cent. The reaction began in both cases at about

65°. The solution clouded at 80°, due to the rapid separation of the halides.

Tertiary Butyl Bromide.—When equal molecular quantities of the alcohol and acid were heated in a flask provided with a return condenser, the yield of bromide was 50 per cent. When the preparation was carried out in the usual way, and twice the theoretical quantity of acid was used, 91 per cent was obtained. The reaction began at about 35°, and at 50° the separation of the bromide was so rapid that the solution clouded.

Tertiary Butyl Iodide.—When the alcohol and the acid were mixed in the ratio of 1 to 3, sufficient heat was produced to cause the separation of the iodide. The yield was 89 per cent of the theoretical.

Isoamyl Bromide.—The effect upon the yield of varying the excess of acid was studied in this case. The alcohol was mixed with one, two, and three times the theoretical amount of hydrobromic acid. The yields were 37, 78, and 85 per cent, respectively. Reaction began at about 105°.

Isoamyl Iodide.—Molecular ratio of alcohol to acid, 1 to 3; yield, 80 per cent.

Allyl Bromide and Iodide.—A sample of Kahlbaum's commercial allyl alcohol was used. The mixtures of the alcohol and acids darkened when heated. With hydriodic acid some iodine was set free. The yields when the molecular ratio of alcohol and acid was 1 to 3 were 61 per cent of bromide and 58 per cent of iodide.

The Action of Hydrochloric Acid on the Fatty Alcohols.—When propyl alcohol was distilled with dilute and with concentrated hydrochloric acid, no chloride was formed. The distillate contained both the acid and the alcohol, and in certain cases appeared to have a constant boiling point. The alcohol was readily separated by adding potassium hydroxide to the distillate. No chloride was formed from isopropyl or isoamyl alcohols. With secondary and tertiary butyl alcohols the results were different.

Secondary Butyl Chloride.—When secondary butyl alcohol was distilled with six times the theoretical quantity of con-

centrated hydrochloric acid, the alcohol distilled over with the hydrogen chloride which was given off when the acid was heated, and no chloride was obtained. In another experiment the solution of hydrochloric acid was of the same molar concentration as the hydrobromic acid used in the preparation of the bromides; namely, one having the specific gravity 1.14, which corresponds to the composition $HCl.5H_2O$. The yield of chloride was 12 per cent, when the molecular ratio between the alcohol and acid was 1:3. Under the same conditions the yield of bromide was 95 per cent. The largest yield of chloride was obtained when 5 grams of the alcohol were distilled with 90 grams of the constant-boiling mixture of hydrochloric acid and water (sp. gr. 1.10). This was 50 per cent. By adding potassium hydroxide to the aqueous part of the distillate, 2.5 cc. of alcohol were recovered. When this was returned to the flask and the distillation continued, enough chloride was obtained to make the total yield 72 per cent of the theoretical. The reason for the greater efficiency of the dilute acid in preparing the chloride is probably the fact that when it is used the mixture can be brought to a higher temperature without loss of alcohol than can be done when the acid is a concentrated solution.

Tertiary Butyl Chloride.—When 5 grams of tertiary butyl alcohol and 37 grams of concentrated hydrochloric acid were mixed, the chloride separated immediately. On distillation the yield of the chloride was 94 per cent.

SIMMONS COLLEGE,
BOSTON, MASS.

INTRAMOLECULAR CONDENSATION OF PHTHALANILIC ACID AND OF CERTAIN ALLIED COMPOUNDS. II.

BY J. BISHOP TINGLE AND B. F. LOVELACE.

THEORETICAL.

In a paper published recently by Tingle and Cram[1] it was shown that succinanilic acid,

[1] THIS JOURNAL, 37, 596 (1907).

$$\begin{array}{l} CH_2CONHC_6H_5 \\ | \\ CH_2COOH \end{array},$$

combines readily with aniline, forming the anilide,

$$\begin{array}{l} CH_2CONHC_6H_5 \\ | \\ CH_2CONHC_6H_5 \end{array}.$$

Phthalanilic acid,

$$C_6H_4\begin{array}{l} CONHC_6H_5 \quad (1) \\ COOH \qquad (2) \end{array},$$

on the other hand, shows an entirely different behavior. Although it was found to be possible to convert it into the anilide by means of aniline, yet the experimental conditions were too rigid to be worked out easily. In general, the acid, in presence of aniline and alcohol, passes over into phthalanil,

$$C_6H_4\begin{array}{l} CO \\ CO \end{array}NC_6H_5.$$

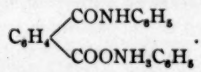
The change is fairly rapid at the ordinary temperature and takes place in a few minutes at the boiling point of ordinary 95 per cent alcohol, *i. e.*, at about 100° below the melting point of phthalanilic acid. We have continued the work of Tingle and Cram and we believe that our results indicate rather clearly the essential mechanism of this interesting condensation. Our work has also opened up a further field for research, but, as we cannot continue the investigation together, we give, in the present paper, an account of our joint results, leaving the continuation of the research to the senior author.

That phthalanilic acid should eliminate water and pass into phthalanil at its melting point is, of course, exactly what would be expected, but why should it do so at the ordinary temperature, or even at 65°? From some of the experiments of Tingle and Cram[1] it might at first appear that the alcohol played an active part in the reaction, because, in several experiments, it was found that phthalanilide could be obtained by heating aniline with phthalanilic acid alone. This idea was disproved in two ways. It was discovered that under ex-

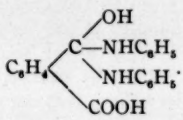
[1] *Loc. cit.*, pp. 601, 602.

perimental conditions apparently identical with the former, though they must, of course, have differed slightly, we could obtain phthalanil from phthalanilic acid and aniline. On the other hand, phthalanilic acid exhibits no change when recrystallized from alcohol. Apparently, therefore, the alcohol simply acts as a solvent and serves to bring the reacting materials into closer contact.

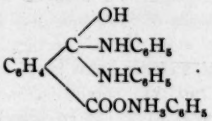
Considering next the aniline. It is evident that it might attack the acid in three ways, as follows: (1) The carboxyl group might react so as to yield *aniline phthalanilate*,



By means of a model it can be shown that this substance might well prove to be considerably less stable than the parent acid and, therefore, that it could more easily eliminate water and aniline. (2) The aniline might react with the carbonyl group, yielding the *ortho compound*,



Such a substance would also probably be unstable. (3) Both of the above reactions might occur simultaneously, yielding the salt of the ortho compound,



It appeared to us that the above hypotheses could be easily tested by treating phthalanilic acid with a tertiary base, such as pyridine or quinoline. These, of course, would not attack the carbonyl group but, if they reacted at all, could form only a salt. As is fully described in the experimental portion of this paper, it was found that each of these bases reacts with

phthalanilic acid as readily as does aniline and under similar conditions, yielding, quantitatively, phthalanil.

We think that this proves clearly, and in a decisive manner, that the first of the above hypotheses regarding the mechanism of the inner condensation of phthalanilic acid is the correct one.

Although the problem of chief interest to us was solved in this manner, we thought that it would be worth while to continue the investigation in two directions. On the one hand, we desired to determine the effect, if any, of a change in the nature of the added base, *i. e.*, to ascertain if other bases acted like aniline, pyridine, and quinoline. On the other hand, we wished to observe the effect on the reaction of substituting the phenyl of phthalanilic acid by other groups. Although the experiments which we had planned could not be completed, we think that the results which we have obtained are of sufficient general interest to justify the continuance of the work.

Experiments with Phthal-β-naphthylamidic Acid,

$$C_6H_4\begin{cases}CONHC_{10}H_7\\COOH\end{cases}$$, *m. p. 200°.*

At 65° aniline acts on this acid rather slowly. Treatment with cold 95 per cent alcohol separates the unchanged acid. From the solution, crystals are obtained consisting, apparently, of impure phthalanil.

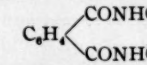
At 100° the action is much more rapid. Two crystalline compounds are separated by means of alcohol. The one appears to be phthalanil and the other phthalnaphthylimide,

$$C_6H_4\begin{cases}CO\\CO\end{cases}NC_{10}H_7.$$

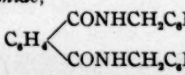
Quinoline is without visible action on the acid at 65°, under the experimental conditions which we employed. At 100° a quantitative yield of phthal-β-naphthylimide is formed.

Pyridine reacts exactly like quinoline at 100°. No experiments were made with it at lower temperatures.

β-Naphthylamine.—In consequence of its relatively high melting point, this base was used in benzene solution. At 65° the acid was not changed. At 100° a portion of the original material was recovered, the remainder being converted into a crystalline compound melting and decomposing at 250°. It is probably phthaldi-β-naphthylamide,

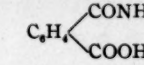


Benzylamine.—Experiments with this base were carried out at 65°, 100°, and 150°–200°. In all cases apparently the same product is obtained. From experiments which are described later in this paper, there can be little doubt that it is *phthaldibenzylamide*,



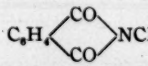
It crystallizes with great ease and melts at 178°–179°. These results will be referred to later.

Experiments with Phthalbenzylamidic Acid,



, *m. p.* 154°.

Aniline, at 65°, yields chiefly phthalbenzylimide,



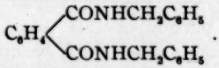
together with a small quantity of crystals melting at 177°. This latter is probably the dibenzylamide mentioned above.

Quinoline failed to react at 65°. At 100° a quantitative yield of the benzylimide is obtained.

Pyridine, at 65°, gave crystals which melted at 119° and were not further investigated. At 100° the yield of phthalbenzylimide was quantitative.

β-Naphthylamine appears to be without action at 65°. At 100° two crystalline products were obtained, but time was not available for their purification. The one undoubtedly consisted chiefly of unchanged naphthylamine and the other appeared to contain phthal-β-naphthylimide.

Benzylamine.—The results obtained with this base were of special interest to us because of the light which they threw on the course of the experiments with benzylamine and phthal-β-naphthylamidic acid. The reaction took place with practically equal ease at 65° and at 100°, and yielded the same product, which we believe to be *phthaldibenzylamide*,



This conclusion is based not only on the conditions under which it was formed, but also on the analysis and on the fact that the substance is not changed by the action of alcoholic sodium hydroxide at the ordinary temperature.

The results described above, although very incomplete, are sufficient to demonstrate that the instability of phthalanilic acid, in presence of aniline, is not peculiar to it, but is a general property of the acids of that series and is brought about by the presence of bases other than aniline. Tertiary bases act as readily as primary ones, consequently the change to the imide must be due, primarily, to salt formation. It is also evident that the course of the reaction is greatly influenced by the nature of the amine employed and also by that of the substituted amidic group which is present. It would appear that the chief factor in the result is the more or less strongly positive nature of the participating groups. On these points it is hoped to throw additional light by subsequent work.

EXPERIMENTAL.

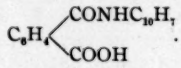
Our experiments were carried out essentially in the manner described by Tingle and Cram.[1] The acid under examination was mixed with the base in question, provided the latter was a liquid, otherwise benzene was used as a solvent. The heating was carried out in a large water bath, which, with very little trouble, could be maintained practically constant at 65°. In the case of the experiments at 100°, the water was, of course, boiled briskly. The experiments are strictly comparable as regards conditions, because a considerable number of them were carried out simultaneously.

[1] *Loc. cit.*

Phthalanilic Acid and Aniline.—These were mixed with the base in excess and heated at 65° during ten minutes. The product was treated with 95 per cent alcohol and the residue was found to consist of practically pure phthalanil, m. p. 203°.

Similar experiments were carried out with *quinoline* and also with *pyridine*, with exactly similar results. As stated in the theoretical portion of this paper, these experiments show that the transformation must be due to salt formation and not to an attack on the carbonyl group of the acid.

Experiments with Phthal-β-naphthylamidic Acid,



Phthalic acid, or the anhydride, was heated with an equimolecular proportion of β-naphthylamine, in an oil bath, until steam almost ceased to be evolved. The residue was then distilled rapidly with a free flame and the solidified distillate pressed on a porous plate. Without further purification this phthal-β-naphthylimide was treated with alcoholic potassium hydroxide, in slight excess. Rather concentrated alkali was employed, but the exact concentration was not, apparently, a matter of much importance. The clear solution was diluted with a little water and acidified with concentrated hydrochloric acid. After cooling, a small portion of the liquid was filtered and tested with more acid. If no further precipitate was produced the amidic acid was filtered, washed with a little water, and recrystallized once, generally from benzene. The yield was almost quantitative. Unless otherwise stated, the time of heating the amidic acid with the base, in the experiments described below, was always two and one-half hours, the other details being similar to those described for phthalanilic acid.

Aniline.—At 65°, the residue insoluble in alcohol consisted of unchanged acid, melting and decomposing at 201°. The alcoholic solution, on standing, deposited crystals melting at 175°–190°. It did not decompose at 220° and appeared to be impure phthalanil. The quantity was too small for complete purification.

The portion insoluble in alcohol crystallized without difficulty at 100° and melted at 201°, but did not undergo decomposition. Analysis:

	Calculated for $C_6H_4\langle{}^{CO}_{CO}\rangle NC_6H_5$.	Found.
N	6.29	6.54

It appears, therefore, to be phthalanil, m. p. 205°. The product insoluble in alcohol crystallized readily and melted at 216°, the melting point of phthal-β-naphthylimide.

Quinoline.—At 65°, the only compound which could be isolated, in presence of this base, was the unchanged acid. At 100°, a practically quantitative yield of phthal-β-naphthylimide, $C_6H_4\langle{}^{CO}_{CO}\rangle NC_{10}H_7$, was obtained. It melted at 215° and agreed in properties with the description of the compound given in the literature.

Pyridine.—In view of the behavior of quinoline, it appeared to be hardly worth while to carry out experiments with this base at 65°. At 100° the acid was transformed, apparently quantitatively, into phthalyl-β-naphthylimide.

β-Naphthylamine.—Owing to its being a solid, the experiments with this base were made in benzene solution. At 65° the acid was recovered unchanged. In the experiments carried out at 100° the product remaining after evaporation of the benzene was treated with cold, dilute hydrochloric acid and the residue washed with alcohol. The insoluble portion consisted of unchanged acid. The alcoholic solution deposited crystals which melted and decomposed at 250°. They consisted probably of *phthaldi-β-naphthylamide*,

$$C_6H_4\langle{}^{CONHC_{10}H_7}_{CONHC_{10}H_7}.$$

Benzylamine.—At 65° a crystalline compound was obtained from the alcoholic washings. It melted and decomposed at 176° and was, apparently, identical with the compound formed at 100°. In the case of the experiments at 100°, only one compound could be distinguished with certainty.

The residue which was not dissolved in alcohol melted and decomposed, after recrystallization, at 174°. It will be further investigated. The solution deposited colorless needles, which melted at 178°–179°. Analysis:

	Calculated for $C_6H_4(CONHCH_2C_6H_5)(CONHCH_2C_6H_5)$.	Found.
N	8.14	8.08

In one experiment the materials were inadvertently heated to about 150°–200°. The chief product consisted of the compound just described, m. p. 178°–179°. In addition, there was obtained from the alcoholic washings a small quantity of a crystalline compound. It melted at 165° and was not obtained in quantity sufficient for further examination.

Analysis:

	Found.
N	8.69

Experiments with Phthalbenzylamidic Acid,

$C_6H_4(CONHCH_2C_6H_5)(COOH)$, *m. p. 154°.*

This acid was prepared from phthalic acid and also from phthalic anhydride and benzylamine, in exactly the same manner as the β-naphthylamine derivative. Its properties agreed closely with those described in the literature, and the yield was practically quantitative.

Aniline.—At 65° there was obtained a crystalline residue from the alcohol which melted at 177°. The quantity was too small for further purification, but the substance is probably the dibenzylamide. The alcoholic solution deposited crystals of phthalbenzylimide,

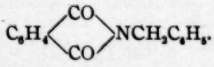
$C_6H_4(CO)_2NCH_2C_6H_5$,

which melted at 116° and agreed in properties with the description of this compound which is given in the literature.

The experiments at 100° resulted in the production of a clear liquid. The addition of alcohol caused the formation

of crystals, which melted at 108°–110°. On allowing the filtrate to stand other crystals were obtained, melting at 166°–169°. Time was lacking for the purification and identification of these compounds.

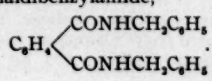
Quinoline.—Apparently the acid is not changed by this base at 65°. At 100° it is converted, quantitatively, into phthalbenzylimide,



Pyridine.—After heating, at 65°, the product was liquid; a little alcohol failed to produce a precipitate, consequently a small quantity of water was added. Crystals, melting at 119°, were formed, but were not further investigated. At 100° a quantitative yield of phthalbenzylimide was obtained.

β-Naphthylamine.—The experiments with this base were carried out in benzene solution. At 65° the acid underwent no change. At 100° two substances were obtained in very small quantity. The portion insoluble in alcohol melted at 180°–185° and, apparently, consisted of impure β-naphthylimide. The crystals deposited from the alcoholic liquid melted at 90°–100° and appeared to be impure β-naphthylamine.

Benzylamine.—Only one compound was isolated in the course of the experiments with this base. It was found in the residue from the alcoholic extraction and also in the alcoholic solution in the case of the experiments carried out at 65° and also with those made at 100°. It crystallizes readily, melts at 178°–179°, and is identical with the compound of the same melting point prepared by the action of benzylamine on phthal-β-naphthylamidic acid (cf. p. 650). These varied modes of formation, its content of nitrogen, and our knowledge of the other derivatives of benzylamine and phthalic acid indicate, with practical certainty, that the compound in question is phthaldibenzylamide,



Confirmation of this formula was found in its behavior towards sodium hydroxide. When treated with aqueous-alcoholic sodium hydroxide it was not visibly changed. The mixture was filtered and the filtrate acidified with hydrochloric acid. No precipitate was formed and the residue, after being washed with water and dried, melted at the same temperature as before the treatment with alkali. Apparently, therefore, the substance is not a salt of phthalbenzylamidic acid.

The work described in the preceding pages was carried out at the Johns Hopkins University. It will be continued and extended under the supervision of the senior author in the Chemical Department of this University during the coming academic year.

McMaster University,
Toronto, Canada,
July, 1907.

OBITUARY.

WILBUR OLIN ATWATER.

Wilbur Olin Atwater, the son of a Methodist clergyman well known in New England, was born in Johnsburg, N. Y., May 3, 1844, and died at his home in Middletown, Conn., September 22, 1907, after an illness of nearly three years. During much of this period of illness he was able to follow to a considerable degree the progress which was made in the lines in which he was interested, but was unable to take part in work of any kind.

He received his academic training at the University of Vermont and Wesleyan University, Middletown, Conn., being graduated from the latter institution in 1865. During a period of post-graduate study at Yale University, which led to the doctor's degree in 1869, he was associated with Professors Johnson and Brewer and had his attention called to agricultural chemistry and the great opportunities this subject offered to investigators. With an insight which characterized him throughout his career, he recognized the future possibilities of such work, and from 1869 to 1871 he studied agricultural and physiological chemistry in the Universities of Leipsic and Berlin. His career as a college teacher began immediately after his return from Europe at the University of Tennessee and Maine State College, and he was called to Wes-

leyan University in 1873, where he held a professorship of chemistry for over thirty years. The first State Agricultural Experiment Station in the United States was organized, largely through his efforts, in Connecticut in 1875, and he was made its first director. Interest in the experiment station movement spread rapidly, and the passage by Congress, in 1887, of the Hatch Act made possible the establishment of such a station in every State and Territory.

In 1894–5 Congress made special appropriations for nutrition investigations under the auspices of the Office of Experiment Stations, and the extended series of publications which have reported this work shows what a large contribution Professor Atwater and his associates have made to this important subject.

Familiarity with the Pettenkofer-Voit respiration apparatus, gained during his stay at Munich, led Professor Atwater to undertake the construction of a similar device, which should, however, include the determination of income and outgo of energy in addition to the income and outgo of matter, and the respiration calorimeter, which was developed by him and his associates, is unrivaled in its class as an instrument of precision, useful for the study of a very large variety of problems connected with physiology and nutrition of man and animals. The bomb calorimeter and the methods of its use were, also, materially improved under his direction.

Professor Atwater's aid was often sought in the study of nutrition problems. As instances may be mentioned the extended investigations of dietetic problems undertaken for the New York State Commission in Lunacy, studies of the nutritive values of alcohol carried on for the Committee of Fifty to Investigate the Liquor Problem, and the series of investigations undertaken for the Carnegie Institution of Washington.

Professor Atwater was a member of many learned societies and received many honors in the United States and Europe. His influence on the development of agricultural education and research in this country and on the study of human nutrition has been of very great and permanent value.

The establishment of the Office of Experiment Stations in the U. S. Department of Agriculture, as a central agency for promoting the interests of the stations, quite naturally followed and Professor Atwater mas made its first director. That this Bureau has in later years followed, with great success, the general policies laid down by Professor Atwater is a proof of his wisdom and foresight.

A long list of articles in scientific and popular journals, in

publications of the Connecticut Storrs Experiment Station and the United States Department of Agriculture, etc., shows the contribution which Professor Atwater has made to the development of agricultural chemistry and agricultural education.

Parallel with his studies in agricultural chemistry, Professor Atwater began early in his career to carry on investigations in physiological chemistry, with special reference to problems of human nutrition. Among his more important earlier work may be mentioned "Studies of Chemical Composition and Nutritive Value of American Food Fishes and Invertebrates," undertaken for the U. S. Commissioner of Fish and Fisheries, and the work undertaken for the Smithsonian Institution and the Massachusetts Bureau of Statistics of Labor. In this and later work, experimental methods were evolved and lines of research outlined which have become generally adopted.

In 1882–3 he devoted considerable time at the Universities of Munich and Heidelberg to familiarize himself with German methods of studying nutrition problems, and later made the study of human nutrition an important part of the work of the Storrs Agricultural Experiment Station, of which he was for many years the director.

A. C. TRUE.

REVIEWS.

POST'S CHEMISCH-TECHNISCHE ANALYSE UNTER MITWIRKUNG VON GELEHRTEN, in dritter vermehrter u. verbesserter Auflage. Von PROF. DR. BERNHARD NEUMANN, in Darmstadt. Erster Band, Zweites Heft. Braunschweig: F. Vieweg und Sohn. 1907. pp. 181–488. Price, M. 7.50.

This contains Chapters V (84 pp.), upon Illuminating Gas, by Dr. Julius Becker, Frankfort a/M; VI (24 pp.), upon Calcium Carbide and Acetylene, by Professor Dr. J. H. Vogel, Berlin; VII (112 pp.), by Professor C. Engler, Carlsruhe, and Dr. Leo Ubbelohde, Berlin, on Petroleum, Tar Oils, Asphalt, and Similar Bodies; VIII (87 pp.), by Dr. W. Fahrion, Höchst a/M, on Fats and Fatty Oils, Glycerine, Soaps, and Candles.

The work is a new edition of the well-known Bolley-Birnbaum-Post "Handbuch," which is similar to Lunge's Chemisch-technische Untersuchungsmethoden. As was noted in the case of this treatise, many of the collaborators have published separate monographs upon their specialties.

While the variety of subjects considered is not as great, nor the treatment of them as complete, as in Lunge's treatise,

yet the book may be cordially recommended to those desiring a clear, concise, and eminently practical handbook, giving the very latest or most approved methods, apparatus, and in many cases references to the literature of the subjects treated.

It has already been noted in a review of sections of this work, which have been previouly issued, that the various parts may be separately purchased on application to the publishers. A. H. GILL.

A TEXT-BOOK OF BOTANY AND PHARMACOGNOSY. By HENRY KRAEMER, PH.B., PH.D., Professor of Botany and Pharmacognosy and Director of the Microscopical Laboratory in the Philadelphia College of Pharmacy; Member of the Committee of Revision of the United States Pharmacopoeia; Corresponding Member of the Société de Pharmacie de Paris, etc. Illustrated with 321 plates, comprising upwards of 1500 figures. Second revised and enlarged edition. Philadelphia and London: J. B. Lippincott Company. 1907. pp. 840.

The appearance of the second edition of Professor Kraemer's book will be welcomed by all who are interested in this subject, either as students, teachers, or technical workers. It is stated on the title-page that the book is intended for students of pharmacy, as a reference book for pharmacists, and as a handbook for food and drug analysts. It is admirably suited to all three purposes. It is most convenient to have in small compass such an authoritative work in this branch of pharmacy.

The principal value of the book lies in the treatment of the botanical side of the subject and especially in the microscopical plates. So far as the chemical aspect of the subject is concerned no special features are to be noted, the material being treated in the usual unattractive routine manner.

A key for the identification of powdered vegetable drugs and foods and a description of the distinguishing histological elements of such powders, covering over 100 pages, will probably prove very helpful and furnish excellent exercises for students of pharmacy. A. S. L.

THE TEMPLE CYCLOPAEDIC PRIMERS. MODERN CHEMISTRY, THEORETICAL AND SYSTEMATIC. By WILLIAM RAMSAY, D Sc. New York: Macmillan Co. 1907.

This is a new edition, in one volume, of the two-volume primer which was published in 1900. A few paragraphs on radium are added to the text, otherwise there seem to be no changes.

Sir William Ramsay has condensed so much matter in this little volume and has expressed it so clearly that it is an excellent book for a student to study in reviewing his work. For a layman it would be difficult reading. E. R.

OUTLINES OF INDUSTRIAL CHEMISTRY. A Text-book for Students. By FRANK HALL THORP, PH.D., Assistant Professor of Industrial Chemistry in the Massachusetts Institute of Technology. Second edition, revised and enlarged and including a chapter on Metallurgy by CHARLES D. DEMOND, S.B., Testing Engineer of the Anaconda Copper Mining Company. New York: Macmillan Company. 1907.

This is not a new edition, but merely a new impression of the second edition of 1905, which was reviewed in THIS JOURNAL.[1]

That a reprint should be required so soon shows that this valuable book is deservedly well received. E. R.

A TEXT-BOOK OF ELECTROCHEMISTRY. By MAX LE BLANC, Professor in the University of Leipzig. Translated from the Fourth Enlarged German Edition by WILLIS R. WHITNEY, PH.D., Director of the Research Laboratory of the General Electric Company, and JOHN W. BROWN, PH.D., Director of the Research and Battery Laboratory of the National Carbon Company. New York: The Macmillan Company; London: The Macmillan Co., Limited. 1907. pp. 338. Price, $2.60 net.

That this book contains a large amount of valuable material, systematically arranged and logically discussed, is clearly recognized by every one. It has undoubtedly contributed its share to the development of modern electrochemistry. All things considered, this is probably the best elementary work on electrochemistry that has ever been written.

The book, however, contains some defects, to which it seems only fair to call attention. The headline on page 40, "The Rise and Fall of the Electrochemical Theory of Berzelius," does not give quite the status of this theory at present. It omits entirely the recent work of J. J. Thomson, which shows that the objection to the electrochemical theory of Berzelius, based upon the chemical resemblance between acetic acid and trichloracetic acid, is without the slightest foundation in fact. Indeed, as Thomson shows, this resemblance in chemical properties is in perfect accord with the theory and a necessary consequence of it.

In discussing transference numbers, it is a little surprising that the old apparatus of Nernst and Loeb should have been used to illustrate the principle employed when at least a half-dozen better forms of apparatus have been devised subsequently.

The discussion of the *hydration* of the ions, on pages 78 and 79, is entirely inadequate in the light of what is known at present, and a number of important investigations in electrochemistry are not dealt with at all. It must, of course, be

[1] **38**, p. 96.

recognized that in a work of limited size many things of importance have to be omitted, and here the author must decide.

The best part of the work is that which deals with electromotive force, and this is excellent.

The work of the translator is admirably done. H. C. J.

DIE KATHODENSTRAHLEN. Von G. C. SCHMIDT, Professor der Physik an der Universität Königsberg. Zweite verbesserte und vermehrte Auflage. Mit 50 eingedruckten Abbildungen. Braunschweig: Druck und Verlag von Friedrich Vieweg und Sohn. pp. 121. 1907.

This little monograph is one of the series "Die Wissenschaft: Sammlung Naturwissenschaftlicher und Mathematischer Monographien." The subject dealt with is one that has been brought into great prominence in the last few years, especially by the work of J. J. Thomson on the electron. An idea of the scope of this booklet can be gained from the following headings, which are taken from the contents: Apparatus for the Production of Cathode Rays; The Discharge in Dilute Gases—Cathode Rays; Change of the Cathode Rays; Cathode Rays in Electromagnetic and Electrostatic Fields; Energy and Velocity of the Cathode Rays; The Zeeman Effect; Determination of E and M; Apparent Mass of the Cathode Particles; Production of Fluorescence by, and the Chemical Action of, the Cathode Rays; Reflection, Absorption, and Spectrum of the Cathode Rays, Canal Rays, etc.

The monograph is clearly written and, for a very elementary treatment of the subject, can be recommended.

H. C. J.

THEORIES OF CHEMISTRY, being lectures delivered at the University of California, in Berkeley. By SVANTE ARRHENIUS, Director of the Nobel Institute, Stockholm. Edited by T. SLATER PRICE, D.Sc., PH.D., F.I.C. London, New York, Bombay and Calcutta: Longmans, Green & Co. 1907. pp. 212.

As the German translation of this work has recently been reviewed in THIS JOURNAL,[1] it only remains to call attention to the appearauce of the English version. H. C. J.

MONOGRAPHIEN ÜBER ANGEWANDTE ELEKTROCHEMIE. VOL. XXVII. ÜBER DIE ELEKTROLYTISCHE GEWINNUNG VON BROM UND IOD. Von DR. ING. MAX SCHLÖTTER. Mit 18 Abbildungen. Halle a. S.: Knapp. 1907. pp. 50. Price, M. 2.40.

As there is not much to be said of the electrolysis, the author also gives the chemical methods, as well as much interesting information as to the present state of the bromine and iodine industries, some of which may be new to readers of THIS JOURNAL.

[1] **36**, 523 (1906).

Bromine is produced in Germany from carnallite, as a secondary product in the Stassfurt potash industry, and in Michigan, Ohio, and West Virginia from the mother liquors of certain salt works; it is obtained either by electrolysis or by the action of chlorine on bromides, both in Germany and America. At Stassfurt measured volumes of liquefied chlorine are used with measured volumes of the bromide solution, to avoid an excess of chlorine, which leads to the formation of the chloride of bromine. One liter of chlorine, sp. gr. 1.33, sets free 3 kilos of bromine. In Germany, the carnallite mother liquors consist chiefly of magnesium chloride and bromide. The Michigan mother liquors are chiefly alkali halides, but contain 10–15 times as much bromine as the Stassfurt liquors. In some of the German potash works the electrolytic process was given up because it was cheaper, under existing conditions, to utilize the chlorine resulting from the electrolysis of potassium chloride or potassium hydroxide to break down the bromides of the carnallite mother liquors than to market the chlorine and make bromine by electrolysis.

In 1905, 596 tons of bromine were made in the United States and 700 tons in Germany.

Iodine Industry.—In 1905 Chili produced 300 tons of iodine from Chili saltpetre, Scotland and Ireland produced 130 tons, Japan 90, France 50, and Norway 24, from kelp. The mother liquors of Chili saltpetre contain about 22 per cent of sodium iodate, and are treated in lead-lined vats with a solution of mono- and disodium sulphite,

$$2NaIO_3 + 3Na_2SO_3 + 2NaHSO_3 = 5Na_2SO_4 + I_2 + H_2O.$$

The crude iodine is sublimed and is then about 98 per cent pure.

Seaweed is no longer treated by the old wasteful methods. Some processes are based on the fact that if the fresh seaweed is fermented until it begins to rot, in the fermentation alkaline sulphides and hydrogen sulphide are formed from organic sulphur compounds; the hydrogen sulphide reduces the organic iodine compounds to hydriodic acid, which, in turn, acts on the alkaline sulphides, forming alkali iodides, which do not volatilize when the weed is burned. The water formed in the fermentation also contains dissolved iodides. It is claimed that these improvements have tripled the yield from weed.

Electrolytic processes for obtaining iodine from iodides have been patented, but are not, as yet, factors in the production.

E. R.